Project N°: IST-2002-507424
Acronym: ALLADIN

D1.1: Methodology for multi centre trial

List of Partners:
Arteveldehogeschool (B)
Language and Computing NV (B)
Budapest University of Technology and Economics (HU)
Univerza v Ljubljani, Fakulteta za Elektrotehniko (SL)
Zenon SA, Robotics and Informatics (EL)
University of Wales Cardiff (UK)
Multitel ASBL (B)
The Provost Fellows and Scholars of the College of the Holy and Undivided Trinity of Queen Elizabeth near Dublin (IRL)
Országos Orvosi Rehabilitációs Intézet (HU)
Scuola superiore di studi universitari e di perfezionamento Sant'Anna (I)

Document identifier:	D1_1_V5.doc
Version:	1.0
Date:	25/04/2004
Organisation:	Arteveldehogeschool
Deliverable:	D1.1
Milestone:	M1. A detailed scheme for a multi centre trial, including all clinical, technical and user requirements
Workpackage:	1
Task:	-
Dissemination:	Public
Authors:	Jo Van Vaerenbergh, all partners
External Review	Prof .dr. FCJ.Baro Neuropsychiatry WHO Collaborating Centre for Health. Psychological and Psychobiological Factors

Resume

The activities and measures applied for the methodology for multi centre trial carried out in the ALLADIN project are described in this deliverable.

The methodology contains the detailed scheme for a multi centre trial, including all clinical, technical and user requirements

Table of contents

1. The research question

1.1. Facts and theories on outcome measurement in stroke

1.1.1. Clinical experience leading to ALLADIN

Lewis Thomas (1995) describes in his book `The Youngest Science' how medicine evolved from an art into a sophisticated science.[118] He watched his father, a general practitioner who made house calls and wrote his prescriptions in Latin to his days where medicine became a complex ‘evidence based’ driven profession.

At the beginning of the twentieth century, physicians prescribed empirical nostrums, few of which had any biological basis and even fewer were evidence-based in the way we understand this term these days. Now, at the beginning of the twenty-first century, the concept of a scientific physic is no longer a contradiction in terms. However, the incursion of science into clinical practice has not been consistent. There are still some ‘immature’ areas and neurological rehabilitation is one such area. The relatively late development of the science basis of neurological rehabilitation is most unfortunate as neuro-disability is one of the most important healthcare challenges of the future. There are, for example, over 920,000 new stroke cases in Europe, often resulting in very severe levels of disability.[48]

In clinical practice many physical therapies have been developed through clinical experience alone and have a tendency to be based on out-of-date beliefs regarding what does and does not promote recovery.[129] Often, these rationales lead to recommendations that do not withstand further examination. The deficits being treated are rarely clearly specified. Stroke patients, for example, tend to be grouped together according to very broad categories of severity. If, as seems highly likely, therapy should be tailored to specific deficits, it is essential to specify the precise nature of such deficits. Unfortunately, as yet, there is no clear idea of a correct and easy to use taxomony of lesions or impairments.

In the field of neurological rehabilitation there are many ‘schools of thought’ and different approaches to treatment making evidence-based practice complex and difficult. The heterogeneity of studies with respect to patients, research designs, treatments, comparisons, outcome measures, and results, combined with borderline results in many of the trials, limits the specificity and value of any conclusions that can be drawn from them.

Overall however, the trials support the general theory that physical therapy can improve functional outcomes, principally in patients with less severe disability. There is some evidence for a dose-response relationship between the intensity of the rehabilitation intervention and the functional outcome. However, the lack of definition of lower thresholds, below which the intervention is useless, and upper thresholds, above which the marginal improvement is minimal, for any treatment, make it impossible to generate specific guidelines.

Therefore, from a practical point of view, it is very difficult to properly discuss clinical efficiency, either between clinicians or, between clinicians and healthcare policy

makers. For this reason it may be important to allow an acceptable level of therapeutic freedom where every qualified therapist can themselves put scientific evidence in perspective. However, in contrast, neurological rehabilitation with a limited number of primary and secondary sources of evaluation of effectiveness can potentially avoid the debate concerning "which therapy is best" through the development of a tool which can demonstrate quickly they a particular therapy is no longer for a given patient and should be discontinued or changed. This does not suggest the cessation of fundamental scientific investigations for new and better therapies. It does however pave the way for modeling neurological rehabilitation in terms of usefulness and cost-effectiveness.

1.1.2. Theory and literature leading to the conceptual design of ALLADIN

To label a patient with 'stroke' is not useful to guide rehabilitation. Even use of such terms as 'floppy' or 'spastic' are still meaningless in the frame of collaborative therapeutic and functional goal setting. Descriptions such as *"He complains that his arm feels abnormally heavy when it is lifted above his head, highly similar to the sensation of a dead arm and this is resulting in problems when he tries to dress and shave"* are more useful. Such natural descriptions contain a lot of very precise information about a patient. Already more than one thousand such descriptions have been collected during the first three months of the ALLADIN project in listing files (Figure 1).

32	Contraction of the shoulder joint
33	contralateral limb compensatory motions
34	contralateral trunk lean
35	cool
36	coordinated lower limb motion
37	coordination synkinesis
38	correct hand grip
39	counteract extensor spasticity
40	cramp
41	crawling
42	creating a large moment of inertia
43	crook position
44	crook-lying position
45	cross facilitation
46	crossed extension reflex
47	cuff muscles
48	cutaneous sensibility
49	cutaneous stimulation over joints
50	cutaneous stimuli
51	Cylindrical grasp
52	decreased unloading phase
53	decreased weight bearing in the heel
54	Deep sensation
55	deficient muscle tone in the arm
56	degree loss of sensory discrimination is present in the lower limb
57	degree loss of sensory discrimination is present in the upper limb
58	deltoid muscle
59	denial
60	developing extensor spasticity

Figure 1 Natural language descriptions in physiotherapy

If integration of clinical expertise and external clinical evidence is to be achieved, it would be very useful to link these natural language descriptions to a specialized and quantified taxonomy. Once the linking system is developed, all that is required of the therapist is an accurate description of the patient using his/her own words. The therapist can use his/her own language and terminology to quantify the patient.

The ALLADIN clinical standardization software ensures automatic conversion to a general accepted code system linked to the specialized taxonomy. Therefore, every rehabilitation specialist can simply generate the exact operational definition of a patient's status using his own descriptive language during the creation of the rehabilitation report. For a given patient, evaluated at a particular time, the final result must be the same, regardless of the 'school of thought' the therapist/evaluator belongs to.

The creation of such taxonomy is a complex process and will be done in stages. In the case of a stroke patient, the clinical frame is extremely complex. Therefore an accurate and dedicated measuring instrument, the ALLADIN DIAGONSTIC DEVICE (ADD) which covers the entire clinical frame is being developed (see 1.4.2 page 13). This instrument is built in accordance with the latest developments in neuroscience, human motor control and learning. Data clusters generated by this device after the completion of several data mining techniques will be the "hat stand" for a functional directed taxonomy which can be referenced using the natural language descriptions.

As the emphasis in stroke evaluation is on the measurement of task specific activities, ALLADIN uses Activities of Daily Living (ADL) as prime variables for its measurements. The ability to perform task specific activities is the baseline for the well-being of the patient. Evaluation of such functions informs both the patient and the therapist unambiguously about -

1. Realistic goals
2. Current abilities that documents progression toward more complex functional levels
3. Decisions on admission and discharge from a rehabilitation or extended care facility
4. Safety in performing a particular task and the risk of injury.

New findings in basic neuroscience provided the necessary impetus to the ALLADIN research team and helped in the conceptualization of how best to measure these variables with a high accuracy.

The hypothesis is:

"Motor images are endowed with the same properties as those of the (corresponding) motor representations and therefore have the same functional relationship to the imagined or represented movement and the same causal role in the generation of this movement".

The fact that the human brain shows important activity during the simulation of motor actions without physically executing them is important. This means that there is a neuro-psychological relationship between imaging and performing a movement or, that the mental simulation of an action correlates to a subliminal activation of the motor system. This was proven by the use of virtual stimulation to enhance the acquisition of simple motor sequences. It in turn showed that kinesthetic and visual motor imagery and, the actual execution of a particular task share a common neural circuitry. This was clearly demonstrated by a significant increase in motor-evoked potentials over reference values during imagery of the complex movements.

Other results confirmed that this strict parallelism between motor execution and motor imagery and assured investigators that the expected sensory changes when movements are executed can be internally stimulated in the network of motor areas during motor imagery with the same degree of spatial and temporal resolution. This suggests that during the acute phase of recovery, CVA patients can use motor imagery to demonstrate the activity that remains in the partially damaged motor networks; a process that may even facilitate functional reorganization. However, there is an apparent decoupling of sensorimotor cortical and cerebellar areas during imagined movement sequences, suggesting that cortico-cerebellar loops are engaged only when action sequences are both intended and realized. This suggested that besides imagery and movement planning, movement execution must also be part of the ALLADIN diagnostic device. Since, in the first days after stroke, the amplitude of each possible movement is very limited, the idea was developed to use isometric analysis at the start of a functional directed movement. The latter, in combination with movement imagination, is the ideal combination to verify the integrity of a still existing or altered “forward model” for a particular functional task. Six degrees of freedom force torque measurements at the start of each functional task can shed light on the development of new correct or aberrant movement pathways towards functional objects. The start/hold component of the isometric measurement implies not only the analysis of some remaining feedback control capabilities after stroke but also the discovery of any restoration activity in future predictive control loops. The latter is the optimum requirement for human functional behavior. [10-12] [18] [25] [28-32] [38-41] [44-45] [49-52] [54-67] [70] [73-74] [77-81] [86-95] [98-103] [107] [109-117] [120-121] [123][126] [128] [130-133]

1.2. Target population

1.2.1. Characteristics

The stroke population is the focus of the ALLADIN research. Each year there are about 920,000 new stroke cases in Europe. This population is generally an elderly population, but the age for having a first stroke has decreased dramatically. However, it is anticipated that the largest group participating in the trial will be over the age of sixty.

The possible consequences of stroke are many and varied for example paralysis, balance disorders, walking difficulties, perceptual deficits and loss of sensation. Some patient loose the ability to read, recall, think, speak, or otherwise communicate as well as they could before the stroke and can complicate some parts of the research

It is likely that recovery depends on some of these features and is also related to the mechanism, location, and size of the lesion. Recovery is also dependant on the patient's physical capabilities and mental health before the stroke .Depression, which is common after a stroke, may also impede recovery.

1.2.2. Limitations

The patient group recruited for the ALLADIN project will be as representative as possible of the many and varied consequences of stroke. This increases the value of the markers and milestones of recovery. In case of a very limited selected group the discovered markers and milestones would not translate accurately to the more general stroke population.

However, the severity of some perceptual and communicative problems post-stroke may exclude some patients from the investigation group. In any case it is known that this particular group are prone to a bad functional outcome

1.3. The rationales for ALLADIN

1. The rationale for ALLADIN is to create a high level of client centered stroke patient guidance that facilitates responsive, individually appropriate, functionally based goal setting.
2. The rationale is to integrate ALLADIN in formal carry structures and referral processes, in whatever European country, with particular attention to an honestly organized social support.
3. The rationale for ALLADIN is to build a better recognition of the need for physical, social, psychological, vocational and environmental services strategies and to create a fluent exchange between services, guaranteeing the best solution for the individual.
4. The rational for ALLADIN is to put in evidence the importance of environmental, economic, social, cultural and spiritual factors in determining health outcomes.

Those determinants of health can only be taken into account when recovery possibilities are clearly understood. Only then can a realistic discussion about rehabilitation goals take place with a patient (client).

5. The rational for ALLADIN is to build (thanks to new vision and scientific background) the support for the structure of a continuum of services, addressing the changing needs of the patient (client) during the rehabilitation process and over the course of life. The flexible and well thought-out approach inherent to ALLADIN provides a smooth transition between different rehabilitation services and alternative approaches.
6. The rational for ALLADIN is to establish in the rehabilitation system a ubiquitous and general accepted taxonomy built on multiple, readily-identifiable markers and milestones which is easily relayed to the public and to health and social service providers.

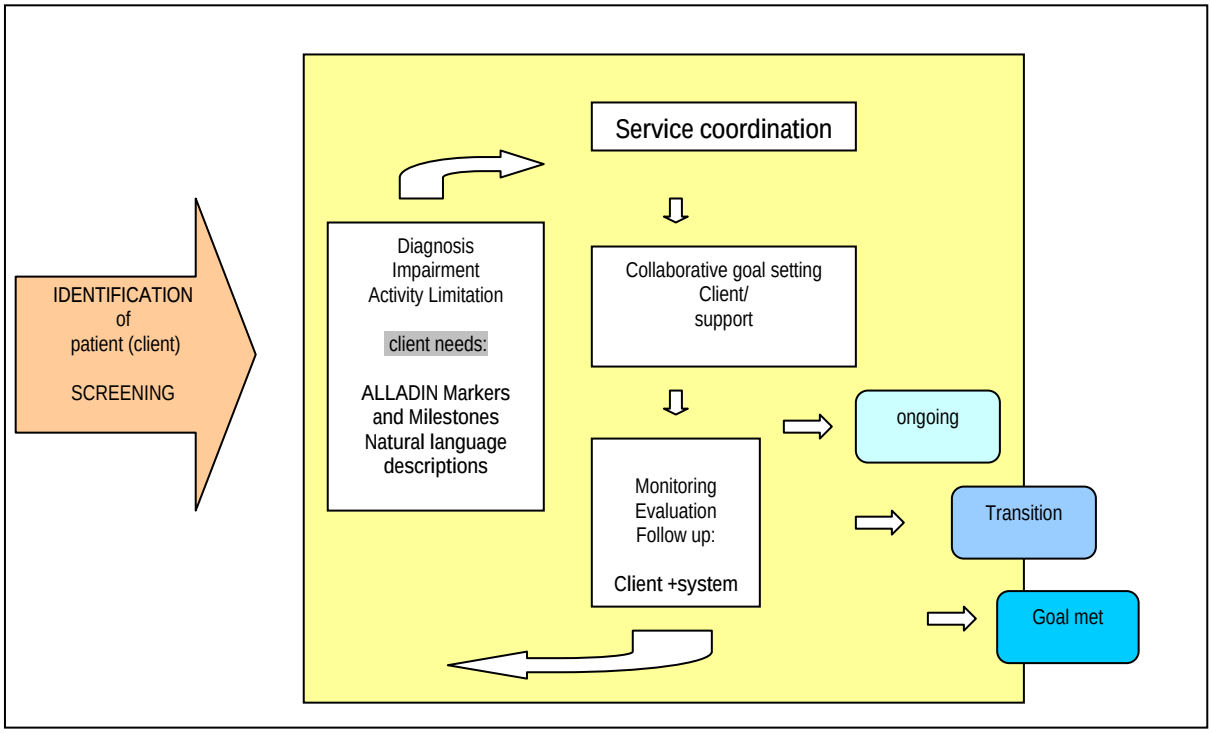


figure 2 Rationales for ALLADIN

1.4. Variables

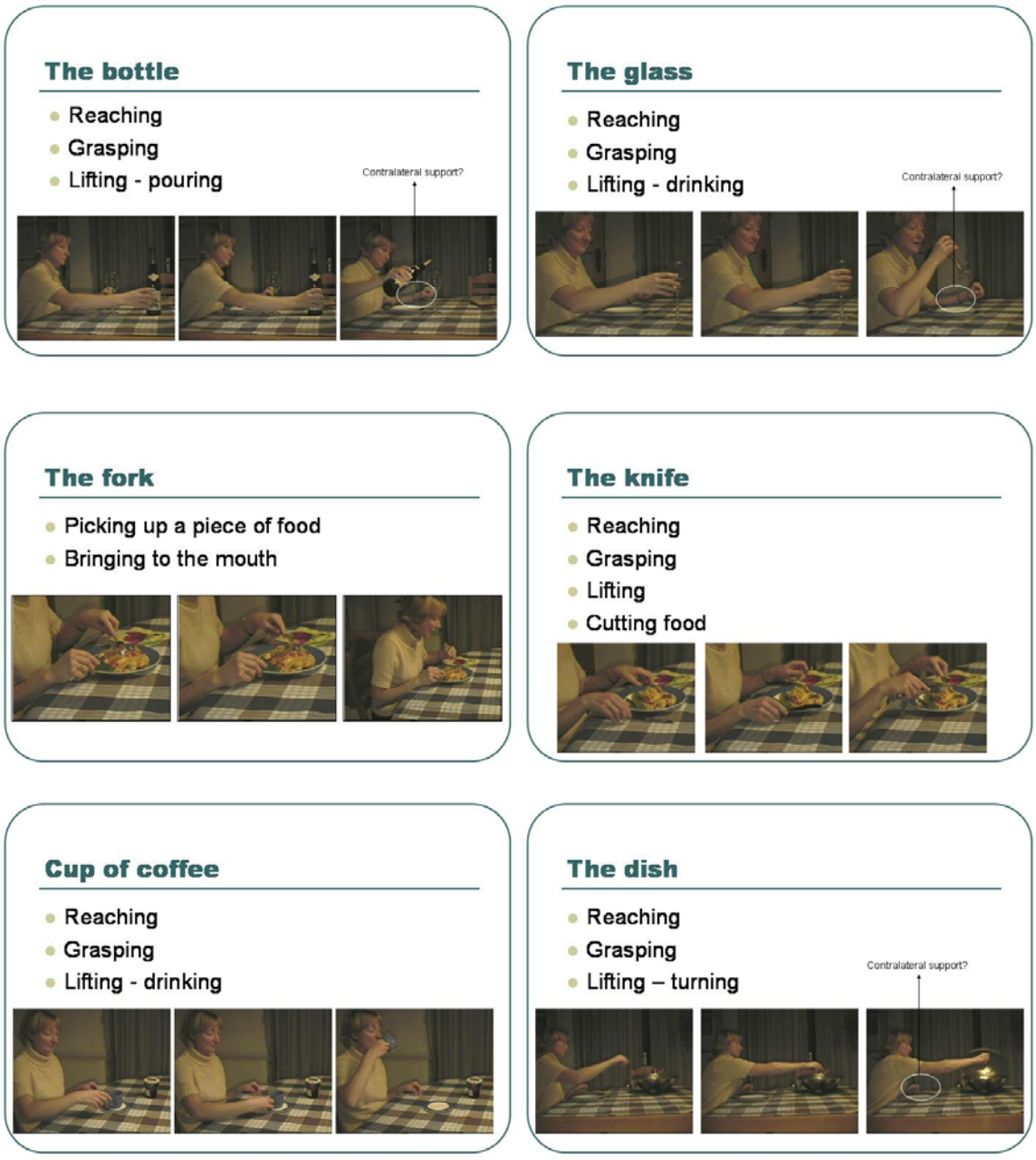
1.4.1. Activities of Daily Living – Choice of tasks

ALLADIN uses Activities of Daily Living (ADL) as prime variables for its measurements because they are indispensable to support the well-being of a stroke patient. The ADL tasks in ALLADIN vary in complexity and cover the whole scope of difficulties in stroke.

Initially **42 possible tasks** were proposed. These were selected after consulting the following textbooks:

1. B. Bobath. Adult hemiplegia: evaluation and treatment [17]
2. M Knott, D. Voss. Facilitation neuromusculaire proprioceptive. Schémas et techniques de Kabat. [71]
3. K. Sawner, J. LaVigna. Brunnstrom's movement therapy in hemiplegia. A neurophysiological approach. [19]
4. J. Carr, R. Shepherd. Neurological Rehabilitation. Optimizing motor performance.[23]
5. C. Perfetti. Der hemiplegische Patient. Kognitiv-therapeutische Übungen. [97]

Figure 3 Daily living functional tasks



Pot laddle

- Reaching
- Grasping
- Lifting and bringing to the center

Pot laddle (2)

- Bringing food to the plate

The spoon

- Reaching
- Grasping
- Turning and bringing to the mouth

The napkin

- Reaching
- Grasping
- Bringing to the mouth

The napkin (2)

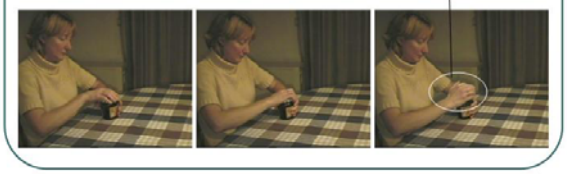
- cleaning

The nut

- Reaching
- Grasping
- Lifting

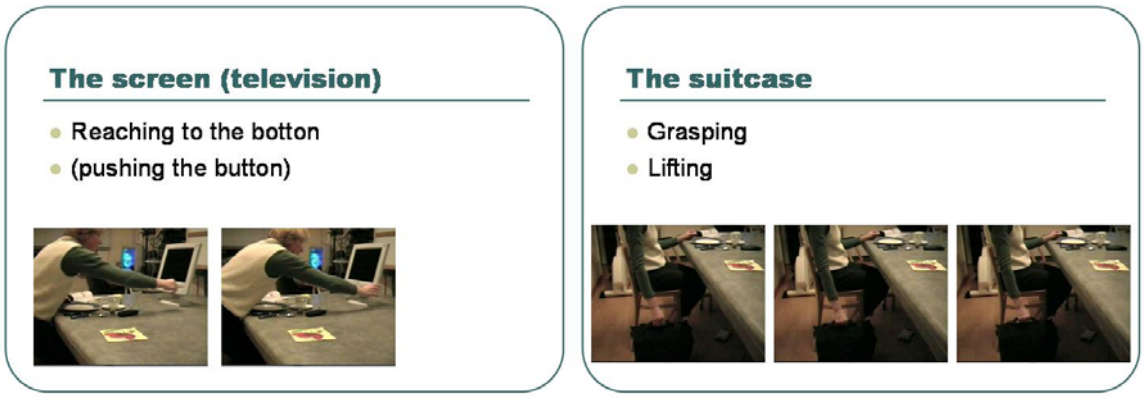
The pot of jam

- Reaching
- Grasping the pot
- Opening the pot



The magazine

- Reaching to page
- Turning a page



Because of time constrains (30 minutes measuring cycle), 6 tasks were finally selected from the 42 formerly proposed. (Table 1) Each task demonstrates features of a reached functional milestone during recovering from stroke.

Lifting a bag
Drinking a glass of water
Taking a spoon
Turning a key
Reaching to a bottle
Lifting and carrying a bottle

Table 1 Selected tasks

1.4.2. Conceptual design of the ALLADIN diagnostic device

1.4.2.1.Isometric force/torque measurements

The simplest way to determine the loads imposed upon the human body from external forces or, to ascertain the forces produced by the muscles, is to measure them externally. Using a commercially available dynamometer the forces (and torques) that are produced at contact points between the human body and the environment can be readily recorded. From the biomechanical point of view, these measurements are the simplest, but provide only a little information about the underlying mechanism within the body. Thus, the highly accurate and reliable data of the force/torque (FT) sensors must be combined with other information from biomechanical studies.
In contrast, the ALLADIN project concentrates on the changes in repetitively measured FT patterns recorded during the imagination and initiation of different Activity of Daily Living (ADL) tasks. Repetitive measurements will be analysed and used for diagnostic purposes only. It is expected that changes in the recorded FT patterns will delineate the course of recovery in stroke and determine the effectiveness of applied physiotherapy in the future. Consequently, a simple isometric FT measurement has the potential to become a convenient and cost effective solution in ALLADIN.

1.4.2.1.1. State of the art of isokinetic/isometric measurements

In recent years, sophisticated uniaxial dynamometers, such as the Kin/Com and Cybex isokinetic **(**constant angular speed**)** dynamometers, have become vailable (although at

exorbitant prices [47]). In addition, a few simple isometric devices (e.g. the Newtest product family) came on to the market. The fixation of the moving elements of an isokinetic device allows for the measurement of isometric FT data. Obviously, in this case, isometric measurements can only be made when a sophisticated and expensive isokinetic device is already present for other purposes. The following subsections of the chapter give a short overview of the existing isokinetic and isometric dynamometers with their main features.

1.4.2.1.1.1 Isostation B-200

The isokinetic dynamometer Isostation B-200 (Figure 4) is specially designed for the triaxial FT measurement of the trunk [4]. In conjunction with an EMG system it is used to better understand trunk muscle co-contraction strategies during free-dynamic lifts.
This device allows the researcher or the physiotherapist to control the three-dimensional resistance experienced by the subject as they move through a three-dimensional range of motion.

Note: Generally, isokinetic dynamometers are uniaxial devices, but Isostation B-200 is a notable exception. Using this device, the three joint torques of the trunk can be measured at the same time.

Figure 4. Front (left) and back (right) views of the Isostation B-200 dynamometer

1.4.2.1.1.2 Loredan/LIDO

The Loredan/LIDO isokinetic dynamometer [5] (Figure 5) measures muscular strength (muscle moment or joint torque) during concentric or eccentric exercise. Various attachments can be configured/interchanged to obtain strength measurements from joints during different biomechanical motions. In addition to its role in biomechanics research, this dynamometer was used for musculoskeletal performance assessments on astronaut applicants to NASA's Medical Sciences division during the astronaut interview/selection process.

Note: Only one degree-of-freedom (DOF) FT data could be measured at the same time.

Figure 5. The Loredan/LIDO dynamometer

1.4.2.1.1.3 Kin/Com

The Kin/Com dynamometers [1] measure the dynamic strength capacities of many joints of the human body. These versatile models have isokinetic, passive, isotonic, **isometric,** protocol and sequential patient exercise capabilities. The Kin/Com model 125AP (Figure 6) is, to the best of our knowledge, the only auto positioning isokinetic instrument. Its auto-positioning function enables to store patient positioning information for future measurements. This avoids important set up mistakes.

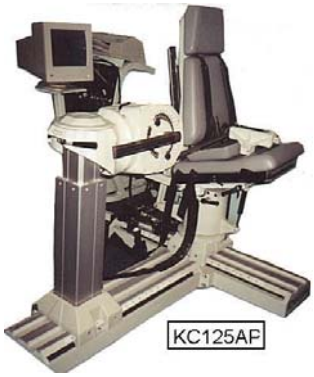


Figure 6. The Kin/Com 125 AP dynamometer

Figure 7 shows the Kin/Com 125 AP dynamometer set up in different positions.

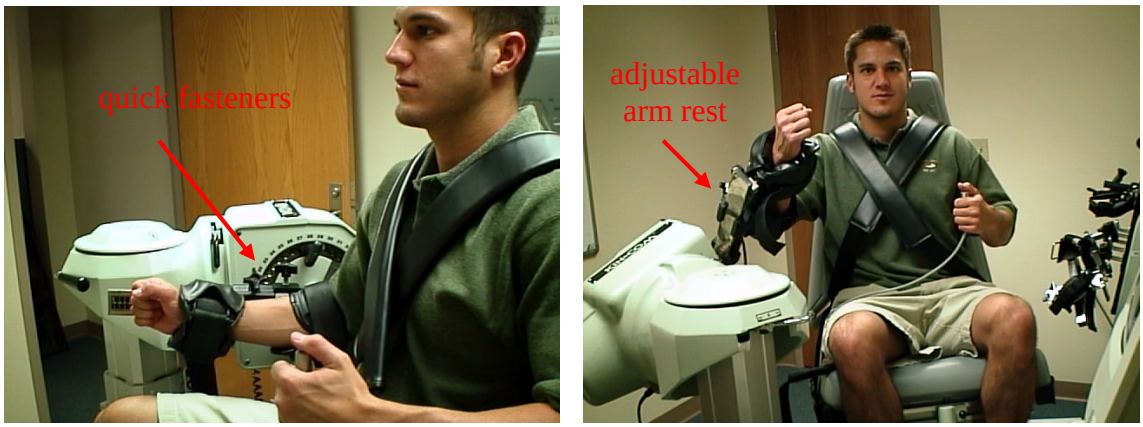


Figure 7. Positioning of the Kin/Com 125 AP dynamometer

Two other Kin/Com models 125E+ and 500H (Figure 8) are available with similar patient exercise capabilities as the Kin/Com 125 AP, apart from the auto-positioning feature.

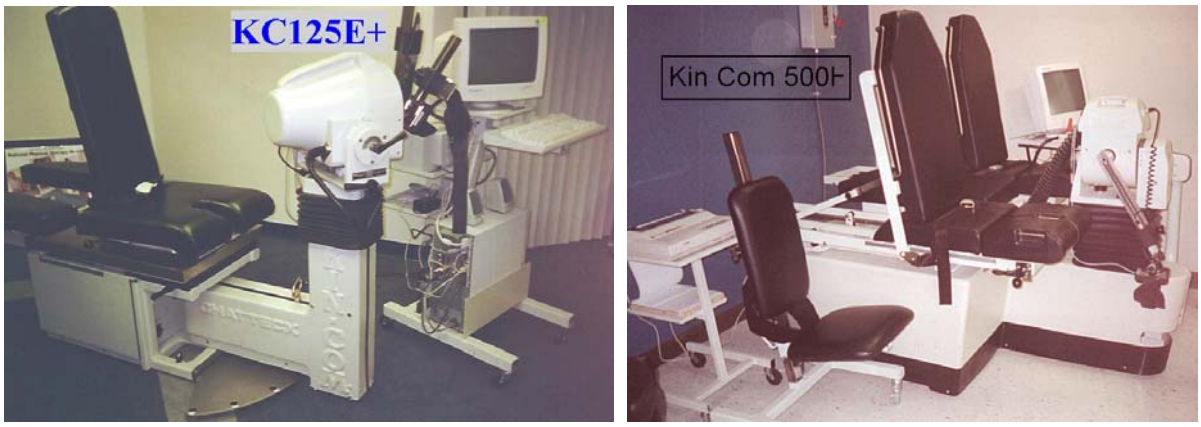


Figure 8. The Kin/Com model 125 E+ and 500H dynamometers

Note: Kin/Com dynamometers are uniaxial devices. Only 1DOF FT data could be measured at the same time.

1.4.2.1.1.4 Biodex – Upper Body Cycle

Biodex – Upper Body Cycle [6] (Figure 9) is an effective total upper body exercise machine. It has wide functional diversity and is ergonomically suited to a wide range of statures and weight. A contoured seat with indexed front-to-back adjustment ensures comfort, safety, and biomechanically correct positioning. The pivoting actuator allows precise vertical positioning of the crank axis (relative to shoulders) for all cyclists, seated or standing. Adjustable-length cranks allow control of shoulder protraction-retraction, torso rotation, and total extremity excursion to avoid pain or to reduce stress to specific tissues. The seat assembly is removable to accommodate wheelchairs or standing cyclists.

The Biodex Upper Body Cycle incorporates two universally accepted and scientifically proven cycling resistance modes in a versatile ergometer that meets the demands of any orthopedic rehabilitation, cardiac, sports medicine, wellness, or general conditioning program. The two resistance modes are: constant power (effort level control) for general aerobic exercises and isokinetic (speed control) for building strength.

Figure 9. The BIODEX – Upper Body Cycle dynamometer

Note: Upper Body Cycle allows only 1DOF torsional resistance.

1.4.2.1.1.5 NORM

NORM (Figure 10) is a multi-joint evaluation and exercise system by CSMI (Computer Sports Medicine Inc.) This isokinetic machine is used to rehabilitate and strengthen patients or athletes while providing quantitative measurement of their performance. It offers isokinetic, isotonic, continuous passive motion (CPM), and **isometric resistance**. Attachments for 22 upper and lower extremity patterns are available.

Figure 10. The NORM dynamometer

Note: In December 2002 CSMI purchased the Cybex Medical product line (including the Cybex NORM). CSMI offers several refurbished Cybex machines.
The NORM dynamometer is limited to a 1 DOF measurement at the same time.

1.4.2.1.1.6 Cybex TEF / TR / LT

The Cybex Trunk Extension/Flexion (TEF), Torso Rotation (TR) and Lift Task (LT) are standalone machines. [2] They are used to evaluate and exercise back extension/flexion, torso rotation and lifting patterns. Figure 11 demonstrates how back extension/flexion is assessed in the Cybex TEF isokinetic dynamometer.

Figure 11. The CYBEX TEF dynamometer

Note: Cybex TEF, TR and LT machines can only measure 1DOF FT data at the same time.

Cybex TEF (similar to other isokinetic devices) imposes artificial motions or loadings on the subject. The subject is forced to move around an artificial axis due to the machine's leverage under isokinetic condition.

1.4.2.1.1.7 Newtest

Newtest Force is a product family [3] consisting of isometric force measuring devices for different parts of human body. Different devices are used to measure trunk extension, flexion and rotation, leg extension, plantar flexion, neck extension and flexion, handgrip and lifting force.

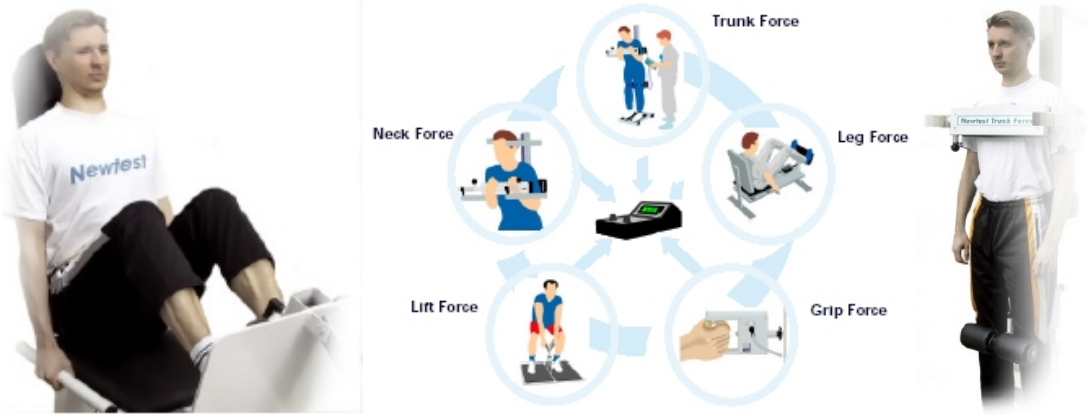


Figure 12. The Newtest isometric force measurement system

Note: All the available Newtest devices measure only 1DOF FT data at the same time.

1.4.2.1.1.8 Conclusion

Isokinetic devices can isolate particular joints to determine the strength requirements of certain motions or the maximum voluntary contraction forces of specific muscle groups. From the biomechanical point of view, they provide adequate information on the joint forces and torques exerted by (or loading) the patient.

However, one of the major shortcoming of these devices is that they impose artificial motions or loadings on the subject by, for example, measuring moments of force under isokinetic conditions or by forcing the subject to move around an artificial axis due to the machine's leverage system. Another drawback is that they can only measure 1DOF FT data at the same time.

In contrast, the ALLADIN Diagnostic Device should be able to measure multichannel isometric FT data in natural start positions. Since the main objective of the ALLADIN project is to find quantitative evidence for recovery during rehabilitation, the implementation of naturalness and synchronous multichannel FT data recording is essential.

There are no commercially available isokinetic or isometric devices on the market that meet the special requirements of the ALLADIN project.

1.4.2.1.2 Functional requirements of the ALLADIN diagnostic device

The ALLADIN diagnostic device (ADD) should be capable of measuring isometric FT trajectories during the imagination and initiation of the selected ADL tasks. Stroke patients, will be invited to perform six different ADL tasks in a prescribed order. The isometric FT patterns will be simultaneously measured by 6-axis FT sensors at different body segments during the imagination and initiation of each ADL task.

The main objective of the isometric FT measurements (and also of the ALLADIN project) is to obtain quantitative evidence for recovery from stroke during rehabilitation. The ALLADIN project will prove that there is synchronism between the change of the recorded isometric FT trajectories and the natural language descriptions acquired about the same time. Every isometric measurement is used to determine the actual status of the patient. Therefore, it is necessary to measure a large number of patients with the same device and, in the same anatomical starting position. This will result in high reproducibility during the entire evaluation period.

The data acquisition system will record isometric FT data from:

- the trunk (at the patient's back)
- the lower trunk (at the patient's fundament)
- the impaired lower arm,
- the impaired foot and toe,
- the impaired middle finger, index finger and thumb.

Note: The above classification of the isometric measurement refers only to the location of the FT sensors.

ADL tasks to be performed during isometric FT measurements in the ADD are listed in the sequence of test administration:

1. *Lifting a bag*: start position[1] of the arm: at side of the body, elbow in natural position (slightly flexed), hand, and foot positions are standard, finger positions as normal (cylindrical grasp). *Object*: a bag placed on the ground
2. *Grasping a glass (no reaching)*: arm is placed close to the body, close to the mid line, foot position is standard, finger positions prepared for a cylindrical grasp. *Object*: glass placed close to the hand
3. *Grasping a spoon*: start position is the same as for grasping the glass. Reaching towards the spoon and opening of the hand is measured. The middle finger should also be measured, foot position is standard. *Object*: spoon is placed a bit higher than the glass and on the side of the back of the hand
4. *Turning a key*: start position is the same as for grasping the glass. *Object*: key in a lock located in front of the hand. The key should be oriented horizontally in the lock
5. *Grasping a bottle*: start position is an almost extended arm over the midline. Start position of the hand is the same as for grasping the glass. Foot position is slided backward, and the back should be leaned forward. *Object*: bottle placed in front of the hand
6. *Bringing the bottle to the other side*: start positions of the arm, hand, and the foot are the same as for grasping a bottle. *Object*: bottle placed in front of the affected shoulder at arm reach distance

1.4.2.1.3 Design requirements of the ALLADIN diagnostic device

Design requirements of the ADD come from three different areas. Firstly, standardisation of the measurement should be provided. Secondly, the developed ADD must meet safety standards, as well as medical certification requirements (see in section 1.4.2.1.4). Finally, there are space limitations in hospitals regarding the room where the device will be used and the location where the ALLADIN wheelchairs (conceptual design of the ADD is presented in section 1.4.4.1) will be stored when they are not in use.

Standardisation refers to reliability and validity. The ADD should provide repeatable and accurate results. Given this important requirement, the patient should be precisely positioned to the same set of ADL positions for each of the 34 measurements during the clinical trial.

Some general design requirements are listed below in different categories:

Adjustability

- Adjustability to discrete patient size ranges
  - "design to all" can hardly be realized
  - individual adjustability is not cost effective
- Adjustability to the affected side
- Adjustability to selected arm-hand and leg-foot postures

Space limitation

- Available area: 1.9 x 5 m^2 is a minimum requirement

[1] Detailed anatomical descriptions of the different start positions are presented in 1.4.2.3.2

- Height limits: 2.7 m
- Storage of wheelchairs (3 pieces)

Access

- PT must be able to manoeuvre the wheelchair
- Free access to attachments, controls and patient fixing devices

Time constraints

- 30 minute measuring cycle (i.e. from patient entry to exit)

Delivery

- ADD attachments as building blocks
- Packed flat on euro pallets (1 or 2): 0.8 x 1.2 m^2

1.4.2.1.4 Safety requirements and medical certification requirements

According to 93/42/EEC [26] the ALLADIN Diagnostic Device is a Class I device with measuring function. As a medical device the ADD shall comply with the relevant electrical, human safety, quality assurance, and medical standards (Table 2). We call all of these standards harmonized standards.

EN	Title
EN 475: 1995	Medical devices – Electrically-generated alarm signals
EN 540: 1993	Clinical investigation of medical devices for human subjects
EN 793: 1997	Particular requirements for safety of medical supply units
EN 980: 1990	Graphical symbols for use in the labelling of medical devices
EN 1041: 1998	Information supplied by the manufacturer with medical devices
EN 1441: 1997	Medical devices – risk analysis
EN 1985: 1998	Walking aids – General requirements and test methods
EN 12183: 1999	Manually propelled wheelchairs - Requirements and test methods
EN 60601-1: 1990	Medical electrical equipment - Part 1 : General requirements for safety
EN 60601-1/A1: 1992	Medical electrical equipment - Part 1: general requirements for safety (IEC 60601-1:1988/A1:1991)
EN 60601-1/A2: 1995	Medical electrical equipment - Part 1: General requirements for safety (IEC 60601-1:1988/A2:1995 + Corrigendum June 1995)
EN 60601-1 /A13: 1996	Medical electrical equipment - Part 1 : General requirements for safety; Amendment A13
EN 60601-1-1: 1993	Medical electrical equipment; Part 1: general requirements for safety; - 1. collateral standard: safety requirements for medical electrical systems - (IEC 60601-1-1:1992)
EN 60601-1-1/A1: 1995	Medical electrical equipment - Part 1 : General requirements for safety - 1. Collateral standard: Safety requirements for medical electrical systems (IEC 60601-1-1: 1992)
EN 60601-1-2: 1993	Medical electrical equipment Part 1: General requirements for safety; 2. collateral standard: electromagnetic compatibility; requirements and tests (IEC 60601-1-2:1993)

EN	Title
EN 60601-2-17/A1: 1996	Medical electrical equipment - Part 2: Particular requirements for the safety of remote-controlled automatically-driven gamma-ray after-loading equipment; Amendment A1 (IEC 60601-2-17:1989/A1:1996)
EN 60601-2-35: 1996	Medical electrical equipment - Part 2-35: Particular requirements for the safety of blankets, pads and matresses, intended for heating in medical use (IEC 60601-2-35:1996)
EN 12100-1	Safety of machinery — Basic concepts, general principles for design – Part 1.
EN 12100-2	Safety of machinery — Basic concepts, general principles for design – Part 2.
EN 14121	Safety of machinery — Principles for risk assessment

Table 2 Harmonized standards applied to the design of the ALLADIN Diagnostic Device

We have extracted from these standards the specific requirements and working conditions to be considered for the operation of the ALLADIN Diagnostic Device as follows:

- Exposure to direct sunshine or excessive temperature, temperature of touchable parts must be lower than 41 degrees of Celsius
- Arrangement of cables
- Correctly fixed cable ends
- Protection of the F/T sensors from irregular mechanical effects
- Protection of the F/T sensors from overloading
- Careful maintenance and cleaning
- Electrical safety and grounding
- Disinfection and sterilization
- Biocompatibility of the materials used
- Design for, and protection against, fatigue fracture
- Design for, and protection against, wearing out (mechanical joints,Velcro, etc.)
- Design for, and protection against, unintended disconnection (quick changer, patient fixation, lifting mechanism, etc.)
- Design for easy disconnection (quick changer, patient fixation, lifting mechanism, etc.)
- Protection against accidental injury from sharp edges
- Design of the platform for easy stepping up
- Protection of the platform against accidental slipping
- Design of the mechanical structure for overloading with a safety factor 8 due to the dynamical effects
- Design for the operation with one operator: reach of devices, sequence of operations, lift of weights, etc.
- Design for electromagnetic compliance: no receiver, no emitter
- Protection against fire

To get which is a requirement for medical applicability we have committed to the use of ‘off the shelf’ products, which have medical (or at least industrial) certification, in the ADD.

1.4.2.2.Force/torque (FT) measurement system

1.4.2.2.1 Preliminary isometric FT measurements at the trunk and at the lower arm

Preliminary isometric FT measurements were carried out in NIMR (National Institution of Medical Rehabilitation, Hungary) to determine the required full scales of the FT transducers. The object of the measurements was not isometric force measurement but analysis of the dynamic effects loading the sensor during a full measuring cycle, including patient entry, patient fixation, isometric measurement, and patient exit. Notwithstanding the analysis below we conclude that the most dangerous phase for the sensor is during patient entry.

For isometric FT measurements we used the REHAROB[2] therapeutic system installed at NIMR. One robot of the REHAROB cell was positioned according to the required ADL task and the patient's size as shown in Figure 13. The lower arm of the subject was fixed in the orthosis and it was connected to the robot through a 6-axis FT transducer.

Note: The glass is not positioned as close to the fingers as required in the ADL definition and, the inclination of the back support could not be set to vertical as it will be for the ALLADIN isometric force measurements.

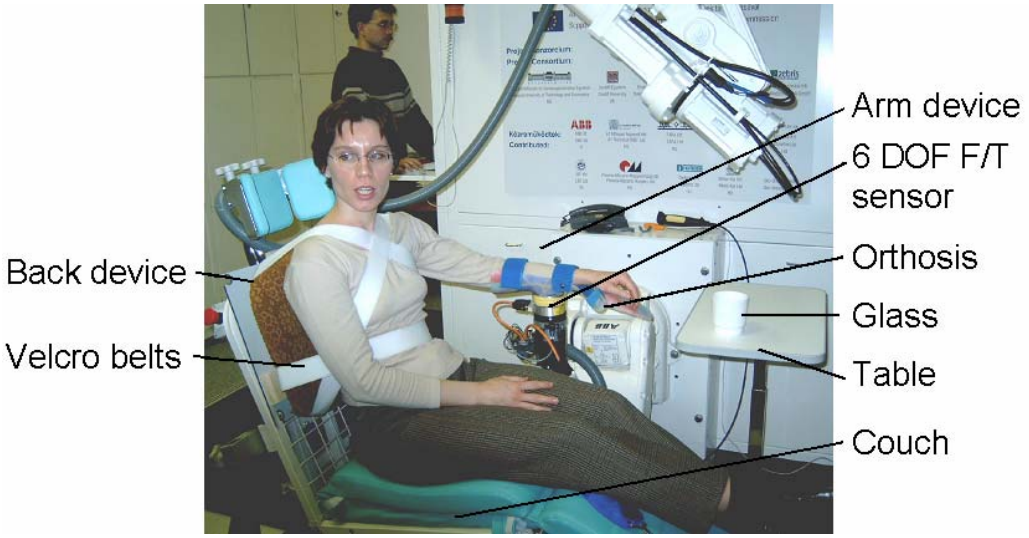


Figure 13 Measurement set-up

Another two FT sensors were used to measure the reaction forces at the back support. The location of the FT sensors and the sandwich structure of the measuring back support are shown in figure 14.

[2] REHAROB is a robotic therapeutic system developed in the 5th framework of the European Union. It provides personalised, three dimensional upper limb motion therapy for the patients suffering from spastic hemiparesis.

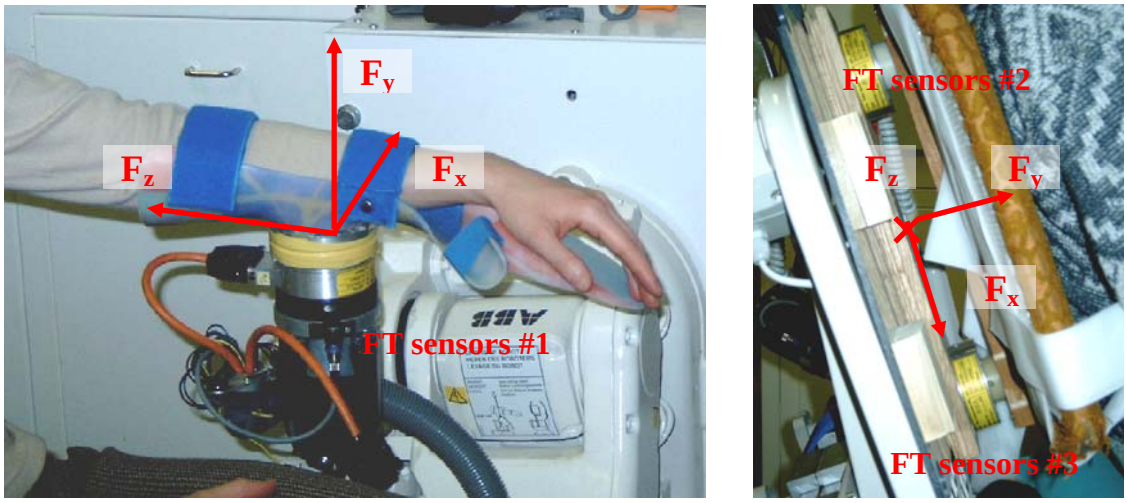
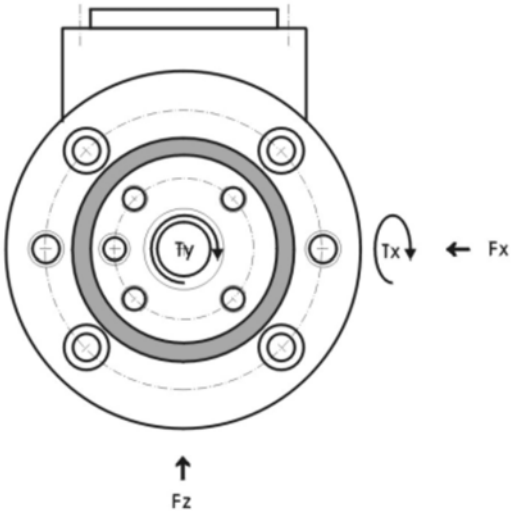


Figure 14 Location of the 6-axis FT sensors

The nominal load capacity of the applied 6-axis FT sensors (type SCT-6/A of A1 Ltd., Hungary) is presented in Figure 14.



F_X = 100 [N]

F_Y = 200 [N]

F_Z = 100 [N]

T_X = 400 [Ncm]

T_Y = 600 [Ncm]

T_Z = 400 [Ncm]

Figure 14b The nominal load capacity of the sensor

During the FT measurements 6 healthy subjects (3 males and 3 females) and 4 stroke patients (3 males and 1 female) were asked to reach for a cup 5 times similarly to ADL2 described in section 1.4.2.5.2.2. The forces and torques loading the sensors were recorded while the subject performed the ADL task and, during the subjects entry and exit. During the trunk measurements the resultant forces and torques were calculated and recorded.

Figure 15 shows the patients entry into the system and addresses the problems associated with patient handling. In the presented case, the physiotherapist must be able to manoeuvre the wheelchair as he/she has to move the patient into the diagnostic device. This must be avoided in the ALLADIN Diagnostic Device for the following reasons:

- Only one physiotherapist should carry out the measurements
- The physiotherapist's workload must be minimised

- Close access to the ALLADIN Diagnostic Device may be difficult with the wheelchair. The ADD will have numerous fixtures around it.
- Sensors can be accidentally overloaded

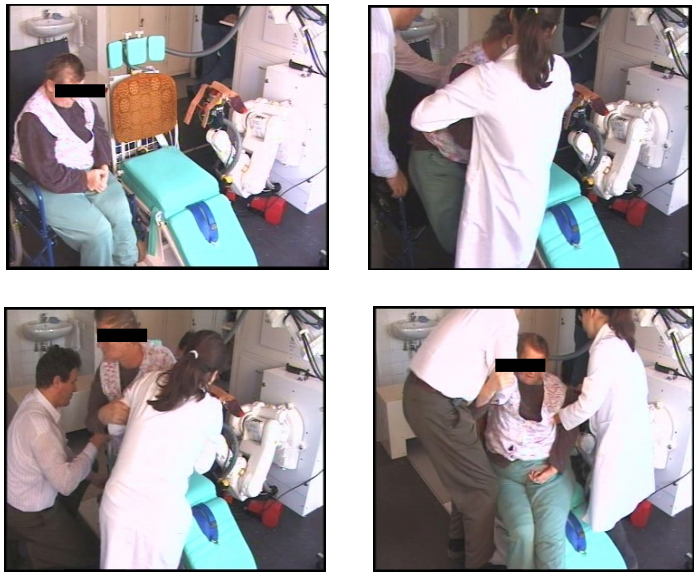


Figure 15. Patient entry to the REHAROB system

Figure 16 and Figure 17 show the measured FT data of the lower arm and the trunk during patient entry. The vulnerable axis of the FT sensors was the Tx axis. The saturation of the Tx signal that can be seen in Figure 17 indicates overload of the sensor. Overloading of the sensors along Tx has not affected the analysis. The reasons for this are explained in the conclusions at the end of this section.

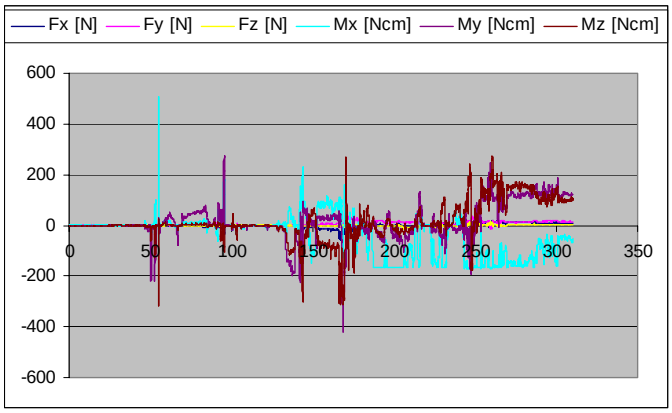


Figure 16. FT data of the lower arm recorded during patient entry

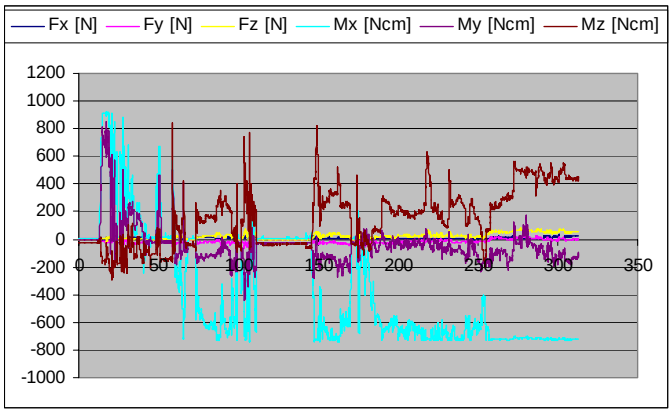


Figure 17. FT data of the trunk recorded during patient entry

The isometric FT trajectories were measured at the initiation of the selected ADL task, which was similar, but not identical to, ADL2. The start position for the performed ADL tests and the location of the object are shown in Figure 18.

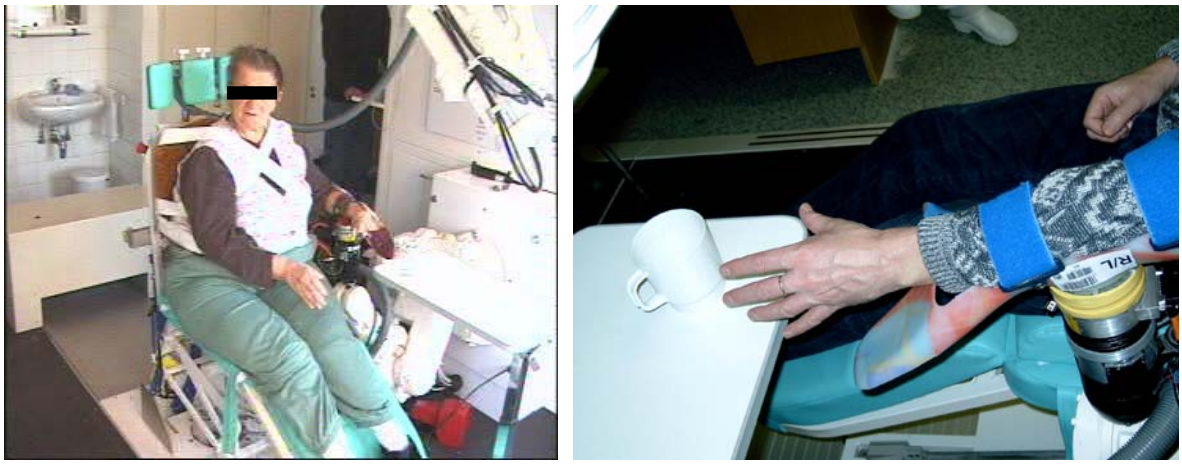


Figure 18. ADL tests (left), location of the object (right)

The FT data recorded during the initiation of the selected ADL task are presented in Figure 19 and Figure 20. The results show clearly that patient entry and ADL tests produces sensor loads in a same order of magnitude. Saturation of the Tx signal illustrates again the overload of the Tx axis of the sensors.

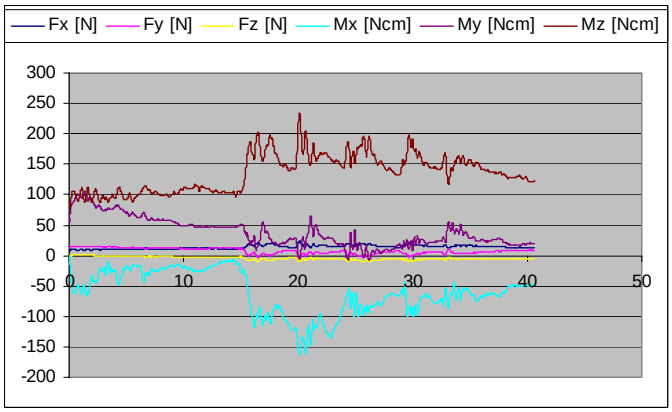


Figure 19. FT data of the lower arm recorded during ADL task

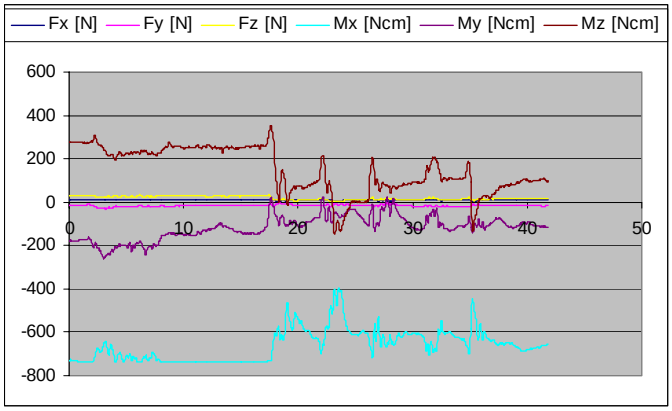


Figure 20. FT data of the trunk recorded during ADL task

The sequence of photos in Figure 21 shows the patient exit from the measuring system. There are some important demonstrable difficulties

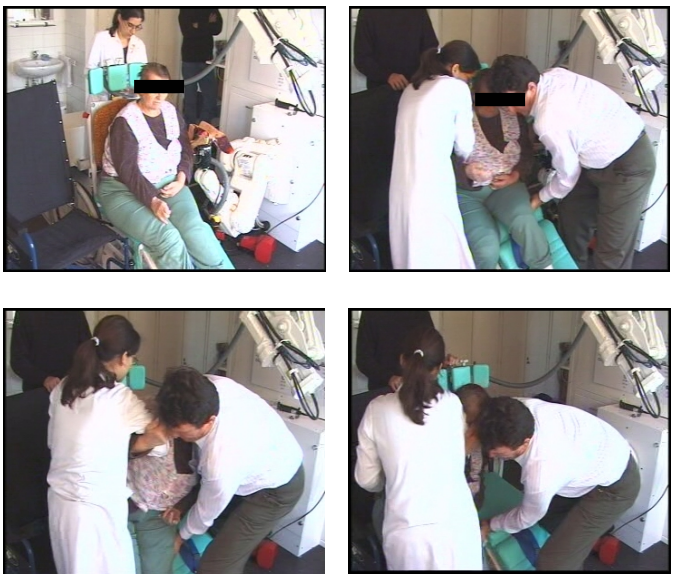


Figure 21. Patient exit from the REHAROB system

The detection of high loads during the patient's exit from the measurement system confirms that patient exit is a crucial phase during which sensors can be accidentally damaged.

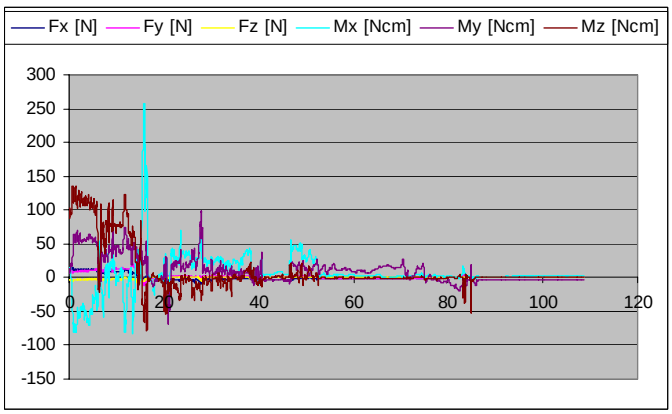


Figure 22. Recorded FT data of the lower arm during patient exit

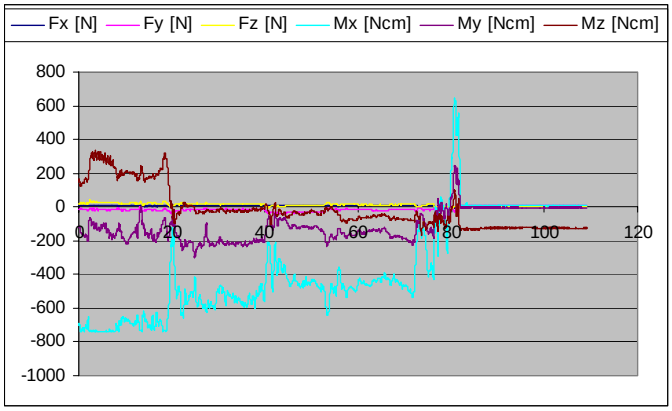


Figure 23. Recorded FT data of the trunk during patient exit

The results of the Max-Min analysis of the preliminary FT measurements of the lower arm and the trunk are summarised in Table 3 and in Table 4, respectively.

Force/Torque	Max	Min
F_x [N]	86.8	-59.1
F_y [N]	68.6	-96.2
F_z [N]	71.5	-73.2
T_x [Ncm]	718.9	-173.5
T_y [Ncm]	668.3	-419.4
T_z [Ncm]	440.4	-316.2

Table 3 Max-min analysis of the lower arm forces and torques

Force/Torque	Max	Min
F_x [N]	77.5	-46.6
F_y [N]	42.6	-168.3
F_z [N]	179.3	-66.7
T_x [Ncm]	918.1	-914.6
T_y [Ncm]	1593.6	-1126.2
T_z [Ncm]	2056	-800.45

Table 4 Max-min analysis of the trunk forces and torques

Based on the preliminary isometric FT measurements we conclude that:

- Considering the possibility of damage to the F/T sensors, entry and exit of the subjects are more critical than the ADL tests.
- Inclination of the backboard used in the provisory measurements unnecessarily increased the load on the F/T sensors. Patient weight is dominant on the loading of the sensors, especially at the inclined back support.
- The trunk device was saturated only along the Tx axis and never along the Tz, and Ty axes. Since the final version of the Trunk device will include a single FT sensor, the maximum values measured along Tz, and Ty well define the required load capacity. It is typical for the 6 DOF FT sensors that the load capacity along Tx is always equal to the load capacity along Tz.
- The provisory measurement set up was adaptable to different patient dimensions.

- Sensor specification is presented in Table 5.

Sensor location	Force [N]	Torque [Ncm]
Arm	±100	±800
Back	±200	±1600

Table 5 Sensor specification based on the preliminary FT measurements

- Sensors should be protected from accidental loading either by overload shields or by engaging the sensors only after the patient is in measurement position.Weight of patients shall be less than 110 kg.

1.4.2.2.2 Requirements for the finger sensors

The three sensors used for the measurement of finger forces should comply with the following requirements:

- The measurement range of the sensor should allow the measurement of loads exerted during the maximal grip force in two fingered grips such as tip pinch, lateral pinch or palmar pinch. The approximate values reported in [83] are:

	Male [F_{max}(N)]	**Female [F_{max}(N)]**
Tip pinch	80 (± 20)	53 (± 11)
Lateral pinch	116 (± 17)	78 (± 11)
Palmar pinch	113 (± 20)	79 (± 15)

Table 6 Approximate values of the finger grip forces

- The maximal load to the sensor is expected to be exerted mainly in the normal direction, although lateral forces should be considered as well, especially during the assessment of patients (e.g. due to contractures). The **force range** of the sensor in the normal direction should allow measurement of forces up to 120N-200N and lateral forces can possibly be expected in the range of 100-150N.
- The required **torque range** of the sensor depends on the leverage of the construction which would fixate the fingers. The advantage is in a smaller-size sensor, which better fits the human hand and reduces the torque range requirement. Assuming a small sensor having 50mm offset and 100N axial load the developing torques for the axes of lateral directions are approximately 5 Nm.
- The sensor should be able to sustain much larger loads exerted to the device during the positioning of the patient in the measuring system.
- The **resolution** of the sensor should be between 0.01N-0.1N,

Given the above requirements, ULFE proposed a sensor having the same (or very similar) characteristic as the Mini45 (SI-145-5) sensor by ATI Industrial Automation. Thus, the main specifications of the sensor are as follows:

Sensing Ranges		**Single-Axis Overload**	
Fx,Fy	± 145 N	Fxy	±5100 N
Fz	± 290 N	Fz	±10000 N
Tx,Ty	± 5 Nm	Txy	± 100 Nm
Tz	± 5 Nm	Tz	± 140 Nm

Table 7 Sensor specification

The **main advantages** of the Mini45 (SI-145-5) sensors are:

- its small physical size (diameter 45mm, height 15.7mm, weight 92g)
- suitable force and torque range
- good ratio between the normal and lateral force sensing ranges (1:2)
- high signal-to-noise ratio
- high strength with very high single-axis overload values (5.4 to 23 times) which should protect the sensor from any physical damage

The sensor has been used previously in finger-force research, robotic hand research and robotic surgery, all of which are good reference sources when considering its capabilities.

1.4.2.2.3 Requirements for the foot and toe sensors

The required full scale measurement range of the foot and toe sensors was determined on the basis of preliminary measurements and partly on the basis of existing references [75], [24], [125], [33]. The references describe experiments completed to study FT produced by the foot during isometric contractions. The measurement apparatus used in the preliminary study at SSSA is shown in Figure 24

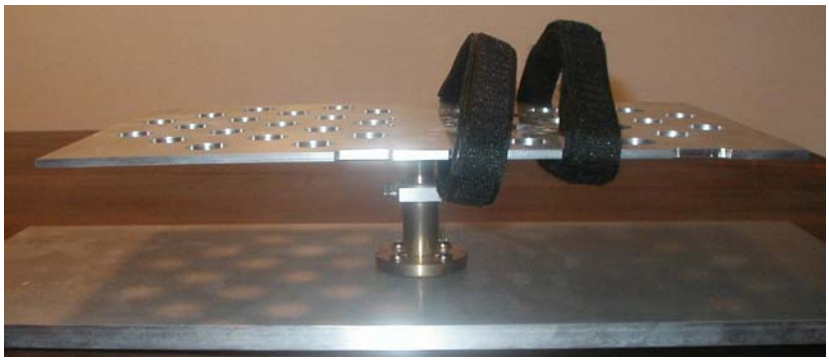


Figure 24 Measurement set-up

During the preliminary experiments one young able-bodied subject of average weight was measured. The subject was seated on a chair and fixed in position with belts. Four sets of measurements were made: on non dominant foot- dominant arm (NDD), on non dominant foot-non dominant arm (NDND), on dominant foot-dominant arm (DD), on dominant foot-non dominant arm (DND). Measurements were done on axis x (lateral), on y (antero-posterior), and on z (normal). Two trials were carried out for each type totalling 24 measurements. The acquisition time was 2 sec. Measurement results are listed in Table 8 and Table 9.

Foot FT sensor	
Lateral forces (Fx,Fy)	300 N
Axial force (Fz)	700 N
Torques (Tx, Ty, Tz)	20 Nm
Dimension	any

Table 8 Proposed measuring range and dimension for the foot FT sensor

Big Toe FT sensor	
Lateral forces (Fx,Fy)	150 N
Axial force (Fz)	150 N
Torques (Tx, Ty, Tz)	5 Nm
Dimension	max Ø50-60 mm

Table 9 Proposed measuring range and dimension for the big toe FT sensor

1.4.2.2.4 Selection of the FT measurement system

For the ALLADIN project a tender was opened for the delivery of 24 (plus 8 reserve components in case of favorable price) pieces of 6-axis FT transducers and the corresponding data acquisition system for use in a medical application.
Candidate manufacturers were selected in a preliminary market research. The best quotation was received from the JR3 Multi-Axis Load Cell Technologies Inc. [7]

The basic characteristics of the selected JR3 6-axis FT transducers together with the short description of the data acquisition system are as follows:
Sensor characteristics

- Number of axes: 6
- Maximal torque and force at the different sensors:

6-axis FT transducers						
Qty.	**Model**	**Description**	**Lateral forces (Fx, Fy)**	**Axial force (Fz)**	**Torques (Tx, Ty, Tz)**	**Dimension**
3	50M31A-I25 150N8	Type-H(and)	150 N	300N	8 Nm	Ø 50 x 31 mm
1	67M25A-I40 150N10	Type-A(rm)	150 N	200 N	10 Nm	Ø 67 x 35 mm
1	90M40A-I50 250N20	Type-B(ack)	250 N	250 N	20 Nm	Ø 90 x 40 mm
1	90M40S-I50 550N50	Type-P(osterior)	550 N	1100 N	50 Nm	Ø 90 x 40 mm
1	90M40A-I50 400N25	Type-F(oot)	400 N	800 N	25 Nm	Ø 90 x 40 mm
1	50M31A-I25 150N8	Type-T(oe)	150 N	300 N	8 Nm	Ø 50 x 31 mm

Table 10. Basic characteristics of the 6-axis FT transducers

- Overload rate: equations for calculations are provided with the sensors.

Data acquisition system

- the ADD will be integrated with a PC, which will collect, compute and store all the measurement data for later use (statistical analysis, data mining).
- the data acquisition system is capable of receiving the force/torque signals of eight 6-axis sensors. It consists of two JR3 Receiver/Processors (model P/N 1593) for PCI bus computers with inputs for 4 sensors.
- Output rate: data can be read from the PCI board at the rate 8 kHz. Data for 6 filters as well as unfiltered data is available at all times.
- Resolution: resolution range is 0.04 – 0.2 N for forces and 0.002 – 0.0063 Nm for torques depending on the sensor type and the current axis:

Resolution of the 6-axis FT transducers

Description	Fx, Fy	Fz	Tx, Ty, Tz
Type-H(and)	0.04 N	0.08N	0.002 Nm
Type-A(rm)	0.04 N	0.05N	0.003 Nm
Type-B(ack)	0.063 N	0.063N	0.005 Nm
Type-P(osterior)	0.1 N	0.2N	0.0063 Nm
Type-F(oot)	0.1 N	0.2N	0.0063 Nm
Type-T(oe)	0.04 N	0.08N	0.002 Nm

Table 11. Resolution of the 6-axis FT transducers

Software

- Component features:
  - transformation of the reference frame (tool transformation)
  - low pass filtering
  - resetting,
  - etc.
- Drivers: Windows 2000 or XP drivers and also ActiveX drivers are provided.
- Application program: The application program will be developed in LabView using Windows 2000 or XP.

1.4.2.3.Anthropometric design

1.4.2.3.1 Design data

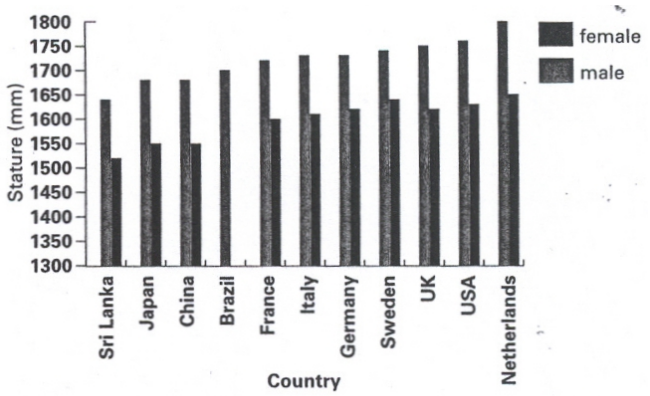
Isometric force measurements require fixed, anatomically standard, and individual setting of the device for all patients. As patient dimensions vary over significant ranges, only a computer controlled positioning system can satisfy these three requirements at the same time. The price and the complexity of such a device are unaffordable. For example, 3 axes at the foot, 3 axes at the arm, and 3x3 axes at the three fingers should be positioned in the case of a sitting patient. In contrast with an expensive mechatronically positioned device we would prefer a simple mechanically adjustable isometric force measurement device. The mechanical positioning should be done with discrete settings because of the measurement standardisation. To study the ideal number and range of those discrete settings we have used the anthropometric design approach in ALLADIN.

In the view of the ALLADIN project we could not recognise important differences between the European populations. International comparison of stature and weight data collected in [9] [96] is presented in Figure 25.

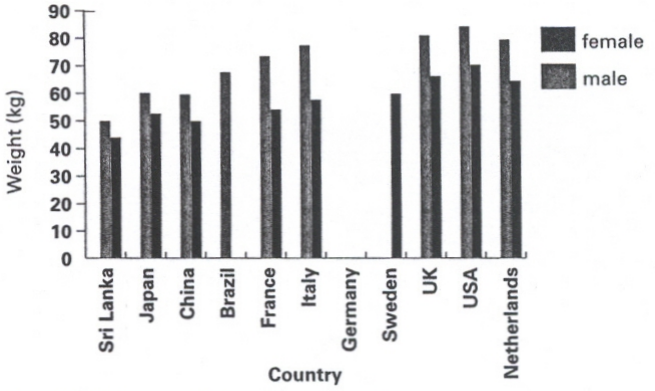
Stature data of the French, Italian, German, Swedish, English and even the American populations are similar, while the weight data of the English and American populations are significantly higher. However, in our opinion, these weight differences have no important role in the anthropometrical design of the ADD. They should be taken into consideration only at the selection of the arm, finger and the foot orthoses or fixtures.

Considering that the largest European population is the German population and, the stature data of this population is approximately the average stature of the above-

mentioned six different populations, the anthropometric design was completed on the basis of this population.



Graph 1: Comparison of stature data



Graph 2: Comparison of weight data

** There are no comparable weight data available for Germany*

Figure 25. International comparison of stature and weight

1.4.2.3.2 Terminology of the anatomical angles

Terminology used in the definition of the anatomical starting positions for the different ADL tasks is illustrated in the following figures.

Joint movements of the upper limb articulations including shoulder, elbow and wrist flexion/extension and elbow hyperextension are shown in Figure 26.

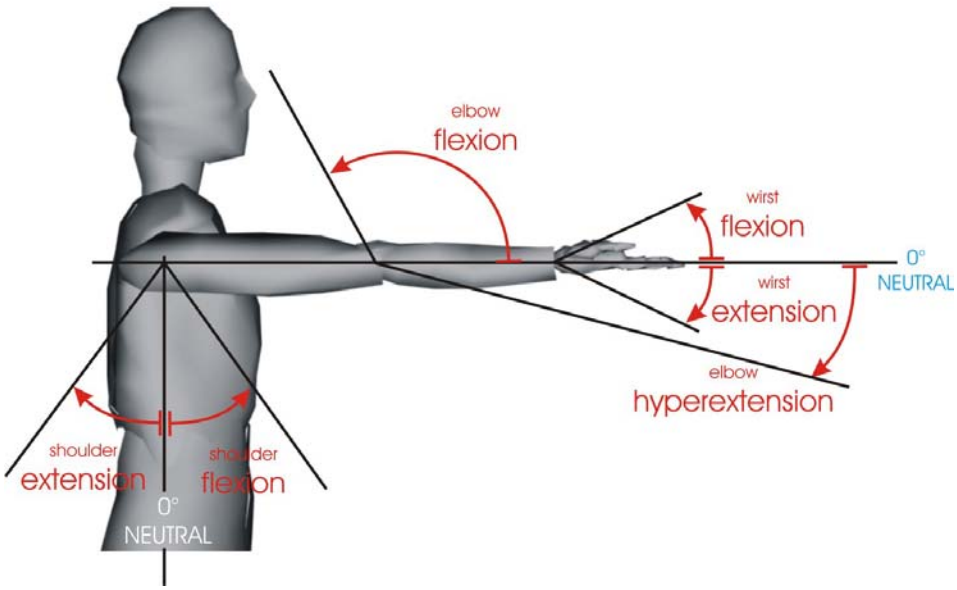


Figure 26. Joint movements of the upper limb articulations #1

Joint movements of upper limb articulations including shoulder abduction/adduction and the radial/ulnar deviation of the wrist are shown in Figure 27

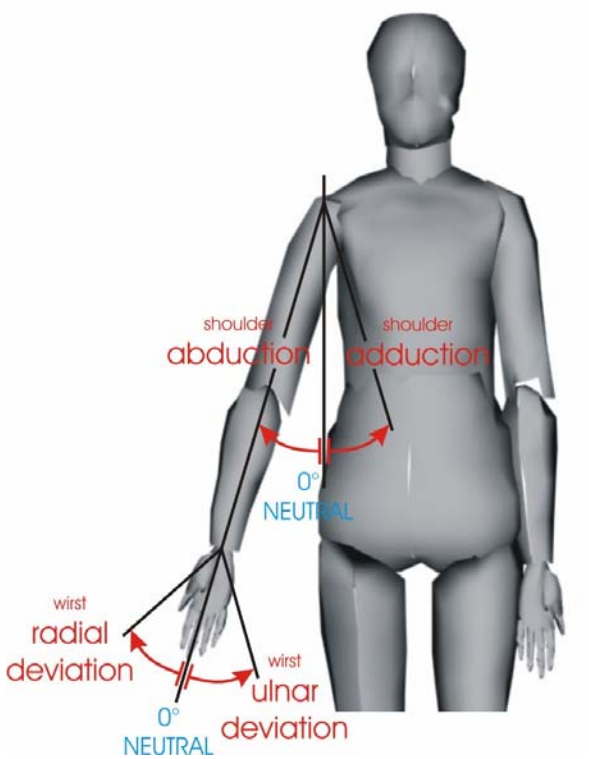


Figure 27. Joint movements of the upper limb articulations #2

Joint movements of upper limb and trunk articulations including shoulder internal/external rotation, lower arm pronation/supination and lumbar-thoracic lateral flexion are shown in Figure 28.

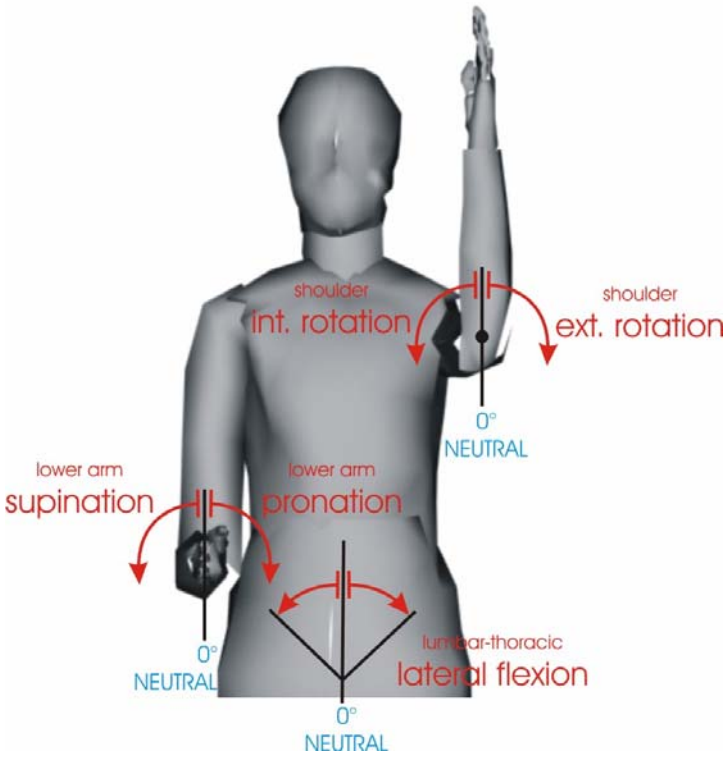


Figure 28. Joint movements of the upper limb and trunk articulations

Joint movements of the fingers including thumb abduction/adduction and finger metacarpophalangeal flexion/hyperextension are shown in Figure 29.

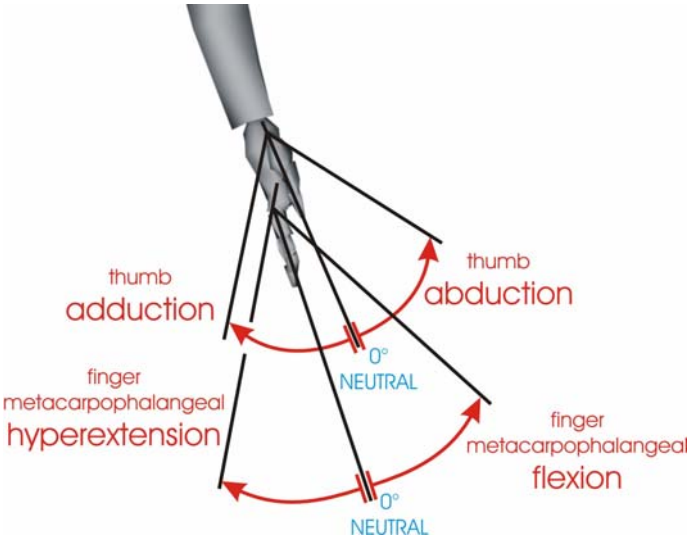


Figure 29. Joint movements of the fingers #1

Joint movements of the fingers including proximal interphalangeal flexion/extension and distal interphalangeal flexion/extension are shown in Figure 30.

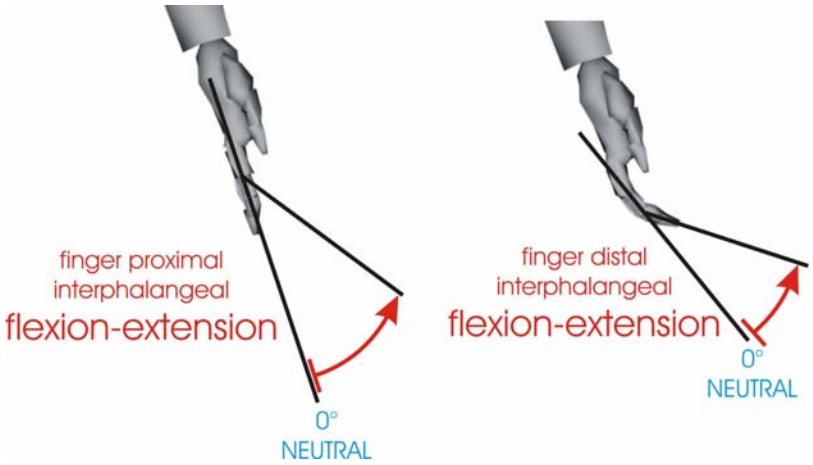


Figure 30. Joint movements of the fingers #2

Joint movements of trunk and leg articulations including lumbar-thoracic, hip and knee flexion/extension, knee hyperextension, ankle dorsiflexion and ankle plantar flexion are shown in Figure 31.

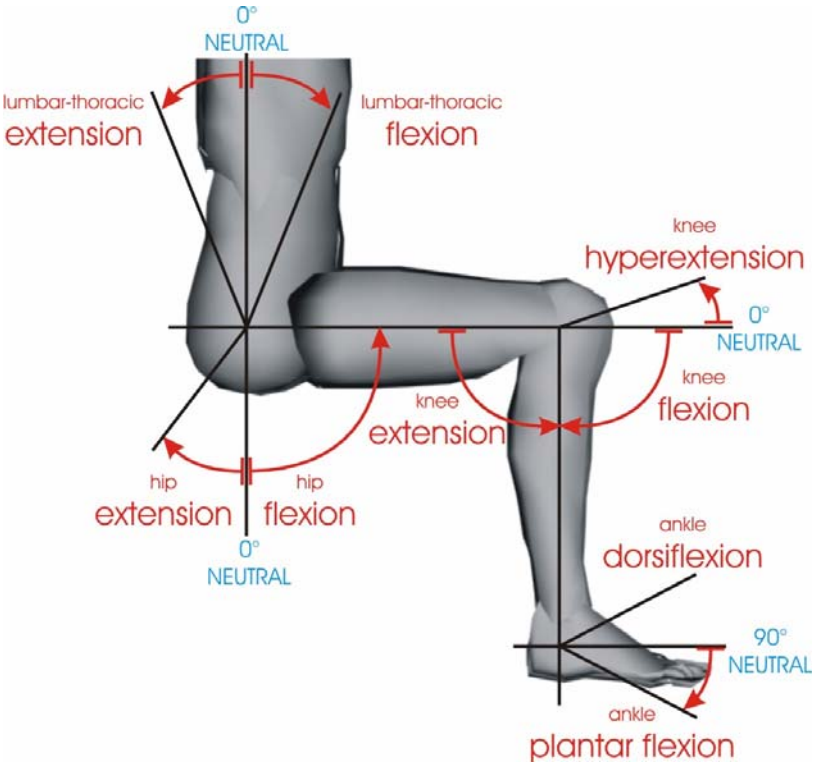


Figure 31. Joint movements of the trunk and the leg articulations #1

Joint movements of the trunk and leg articulations including lumbar-thoracic rotation, hip internal/external rotation and hip abduction/adduction are shown in Figure 32.

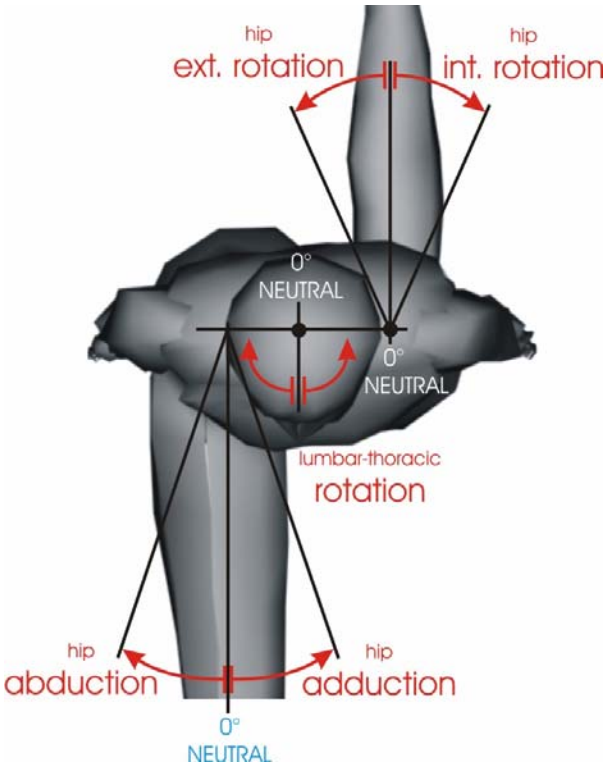


Figure 32. Joint movements of the trunk and the leg articulations #2

Toe metatarsophalangeal flexion, which is the only joint movement of the foot that is taken into consideration, is shown in Figure 33

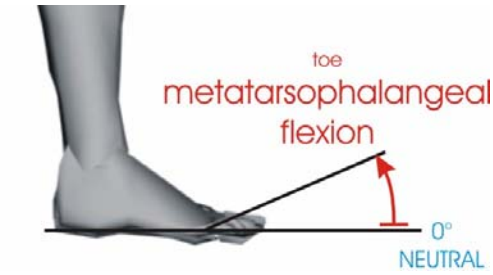


Figure 33. Joint movement of the toe

1.4.2.3.3 Anatomical angles of the selected ADL tasks

ADL tasks have to be performed during isometric FT measurements in three different positions for the 6 selected ADL tasks. The corresponding anatomical angles are listed in tables after each figure that presents a single starting posture.

As a first assumption we propose the percentile[3] values 25%, 50% and 75% for the design of ideal setting of the ADD. This means that the ADD can be set without error

[3] Percentile is the percentage of people in a population who are not larger in that dimension. Percentiles refer to specific dimensions, not whole people.

only to the 25% female, the 50% of the average male and female, and 75% male. We do not recommend males larger than the 95% male and females smaller than the 5% female to be measured with the ADD. As a consequence of the percentile limitation of the patient population during the design of the ADD a patient height limitation will be included in the list of patient exclusion criteria: patients shorter than 1530 mm or taller than 1870 mm will not be accepted for the ALLADIN isometric force torque measurements.

POSITION 1:
ADL task 1 – *lifting the bag*

Note: In the final ADD the wheelchair will not be present during the measurements so collision problems are not expected.
3D mannequin models were created with using the Mannequin Pro tool.[8]

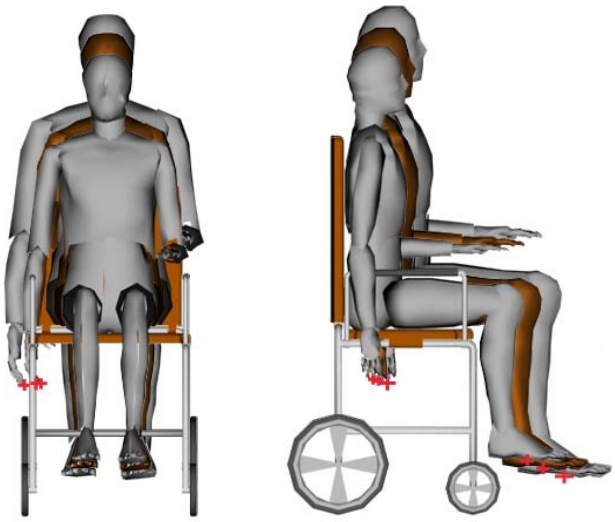


Figure 34. Male patients (%-ile: 5, 50, 95) are sitting in position 1

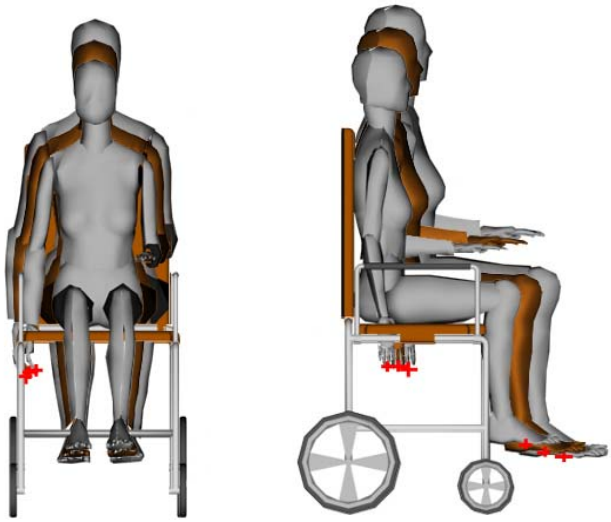


Figure 35. Female patients (%-ile: 5, 50, 95) are sitting in position 1

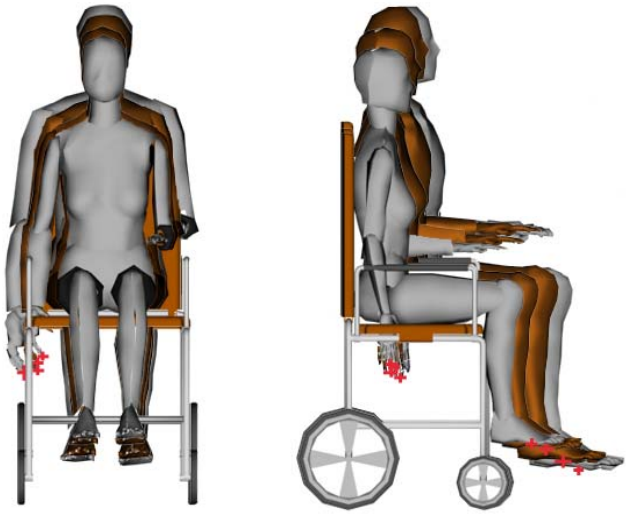


Figure 36 Female (%-ile 25, 50) and male patients (%-ile 50, 75) sitting in position 1

Note:

- the diameter of the front wheel is 160 mm,
- the diameter of the rear wheel is 300 mm,
- the width of the seat is 480 mm,
- the height of the seat is 540 mm,
- the depth of the seat is 400 mm.

The wheelchair is not identical to the B4205 wheelchair presented in the ADD concept. The B4205 transit lying wheelchair (Figure 37) is manufactured by REHAB Inc., Hungary, and selected for the ADD.

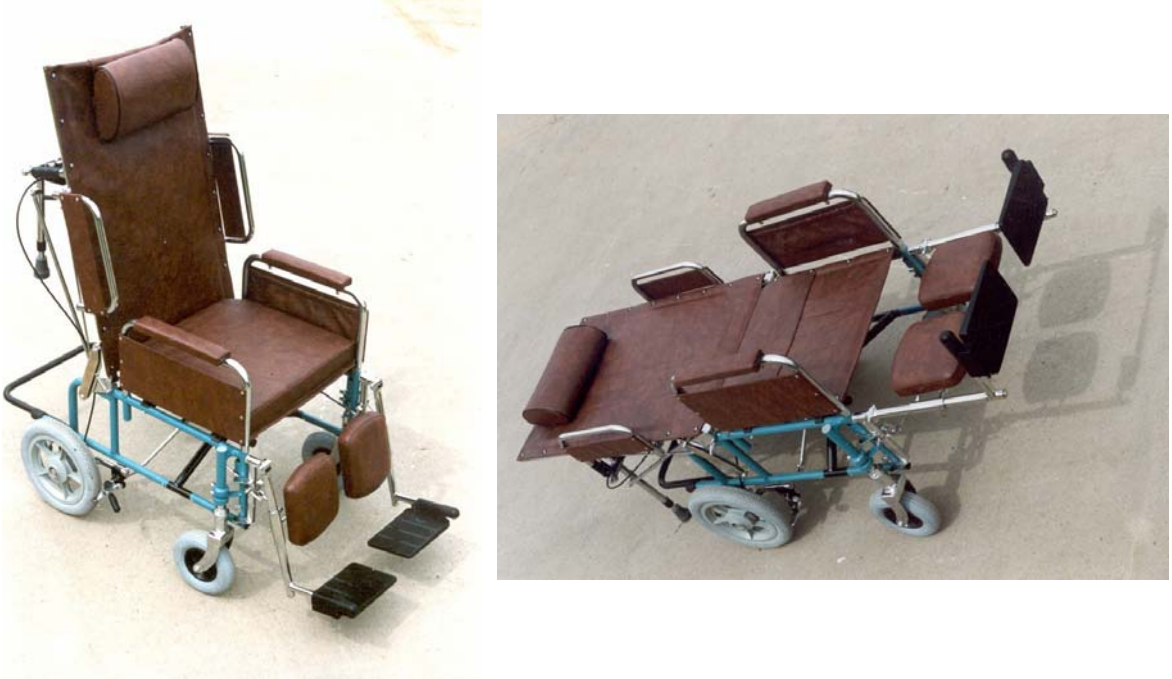


Figure 37. B4205 transit lying wheelchair of REHAB Inc., Hungary

Collision problems arise between the patient's arm/hand and the seat/arm support of the wheelchair. The problem also exists when using the B-4205 wheelchair.

Anatomical angles in position 1 are listed in Table 12, except those that are in neutral position.

Articular movement	Anatomical angles (Male / Female)
Shoulder abduction	5
Shoulder extension	7
Elbow flexion	12
Thumb abduction	50
Finger metacarpophalangeal flexion	15
Finger proximal interphalangeal flexion	20
Finger distal interphalangeal flexion	20
Hip flexion	90
Knee flexion	90

Table 12. Anatomical angles in Position 1

POSITION 2:
ADL task 2, 3 and 4 – *grasping a glass (no reaching), grasping a spoon, turning a key*

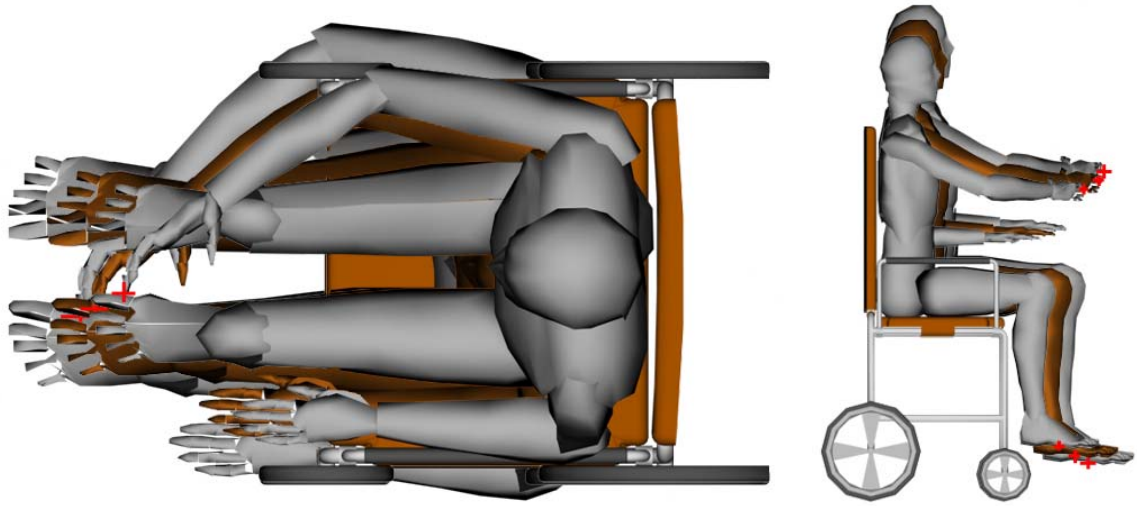


Figure 38. Male patients (%-ile: 5, 50, 95) are sitting in position 2

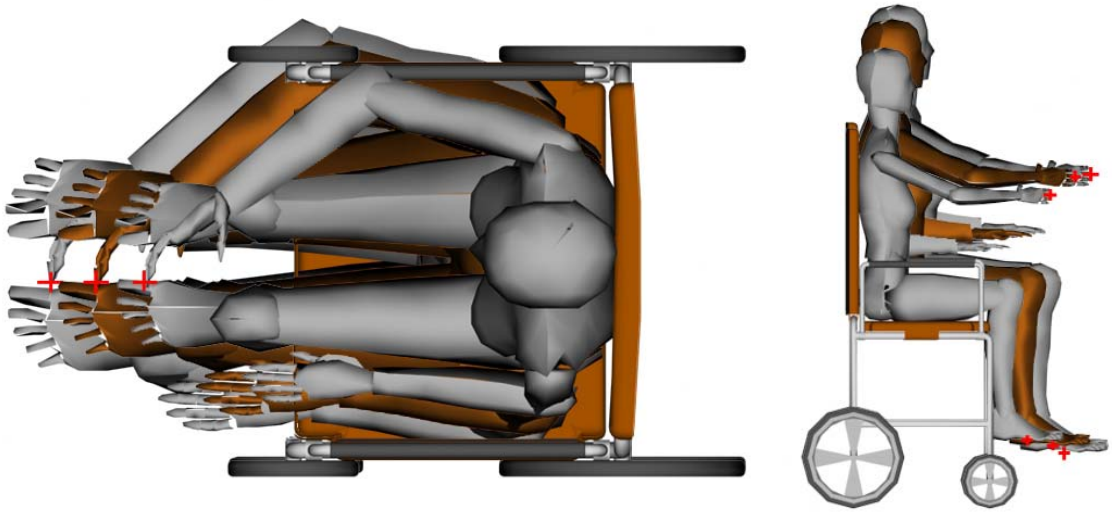


Figure 39 Female patients (%-ile: 5, 50, 95) are sitting in position 2

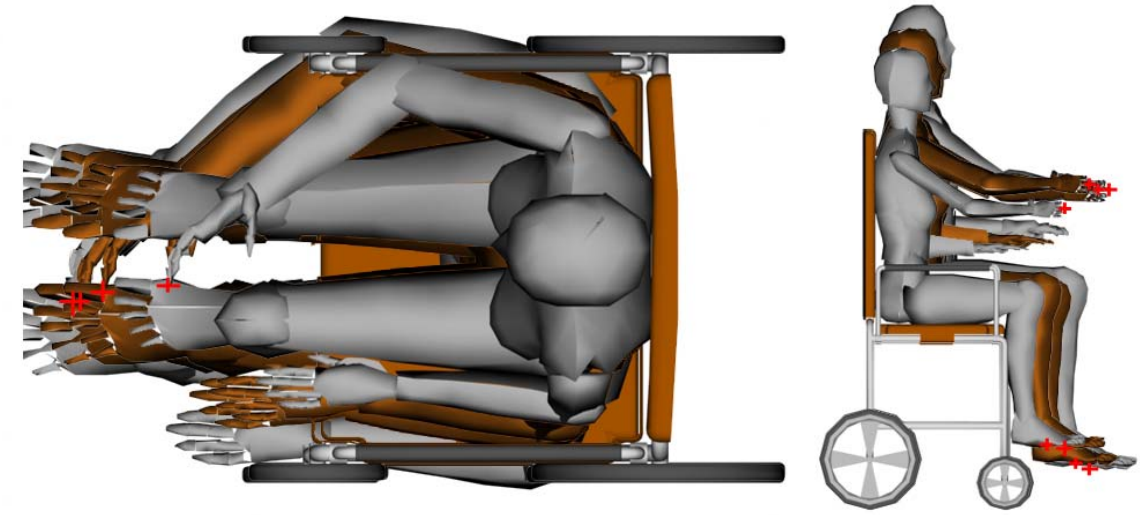


Figure 40 Female (%-ile 25, 50) and male patients (%-ile 50, 75) sitting in position 2

Anatomical angles in Position 2 are listed in Table 13, except those that are in neutral position.

Articular movement	Anatomical angles
Shoulder abduction	15
Shoulder flexion	50
Shoulder internal rotation	45
Elbow flexion	35
Thumb abduction	50
Finger metacarpophalangeal flexion	15
Finger proximal interphalangeal flexion	20
Finger distal interphalangeal flexion	20
Hip flexion	90
Knee flexion	90

Table 13. Anatomical angles in position 2

POSITION 3:

ADL task 5 and 6 – *grasping the bottle, bringing the bottle to the other side*

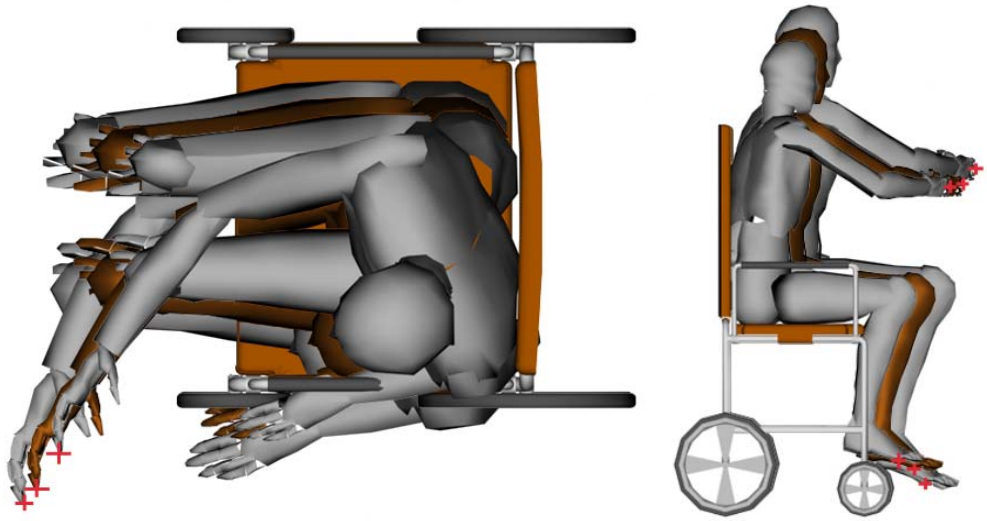


Figure 41. Male patients (%-ile: 5, 50, 95) are sitting in position 2

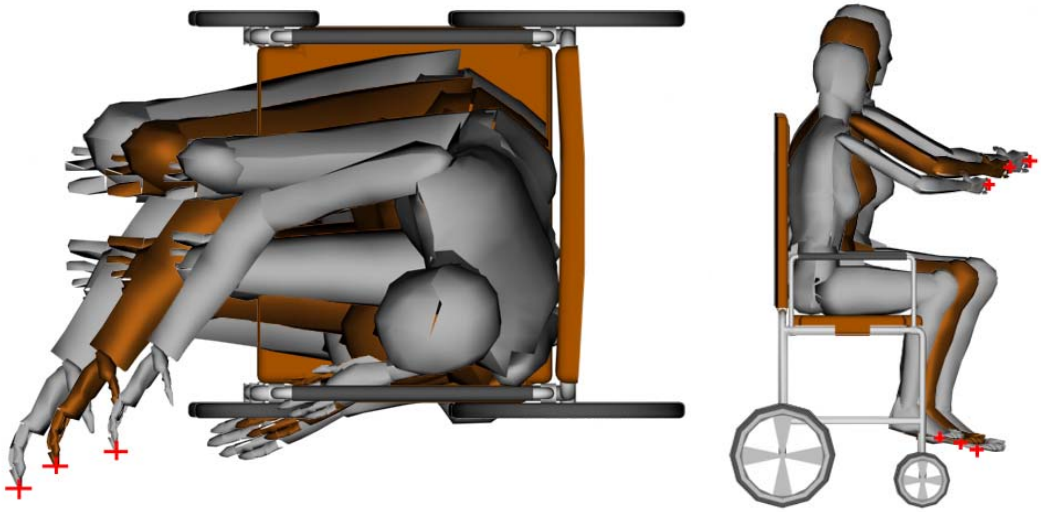


Figure 42. Female patients (%-ile: 5, 50, 95) are sitting in position 3

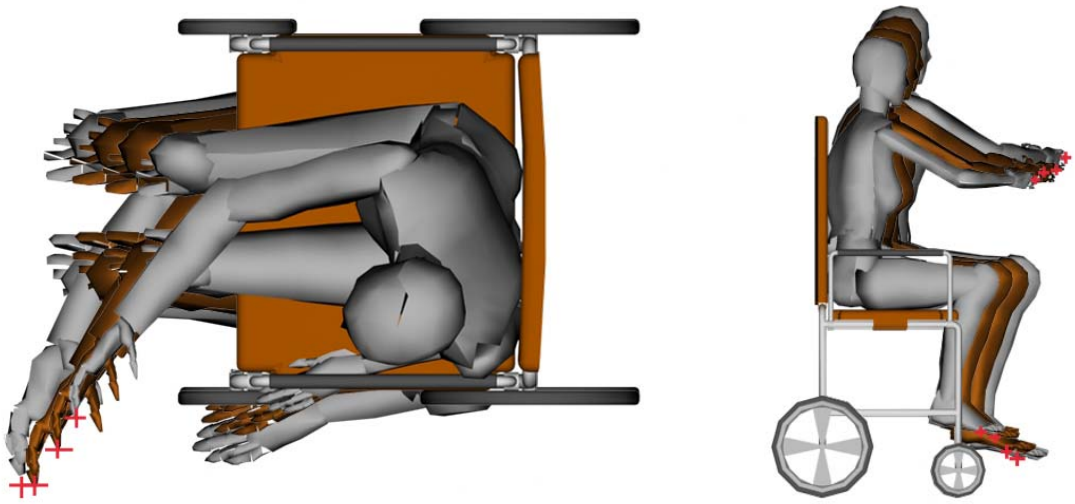


Figure 43. Female (%-ile 25, 50) and male patients (%-ile 50, 75) sitting in position 3

Anatomical angles in position 3 are listed in Table 14, except those that are in neutral position.

Articular movement	Anatomical angles
Shoulder flexion	70
Shoulder internal rotation	45
Elbow flexion	35
Thumb abduction	50
Finger metacarpophalangeal flexion	15
Finger proximal interphalangeal flexion	20
Finger distal interphalangeal flexion	20
Lumbar-thoracic flexion	15
Lumbar-thoracic rotation	20
Lumbar-thoracic lateral flexion	18
Hip flexion	90
Knee flexion	105
Ankle dorsiflexion	8
Toe metatarsophalangeal flexion	7

Table 14. Anatomical angles in Position 3

1.4.2.4.Operational definitions including delineation of tools and procedures

The mechanical design of the ALLADIN Diagnostic device is affected by a set of design criteria.

The first set of the criteria is concerned with the proper setting of the device to the six selected ADL tasks and individual patient dimensions. The anthropometric design approach was used to fit the ADD design to this first set of criteria.

The second set of design criteria is concerned with patient handling. Preliminary isometric force measurements demonstrated that both flaccid and spastic stroke patients can be moved with difficulty. It is assumed that all patients selected for the ALLADIN clinical trial have limited mobility so they are brought to the ADD in a wheelchair. The ADD will be designed so that the physiotherapist can easily move the patient from the wheelchair to the ADD. Furthermore, not only are the difficulties associated with patient transfer mentioned here as a design criterion but the physical effort associated with transfer from the wheelchair to the ADD and, the comfort of both patient and physiotherapist throughout must also be considered. One possibility is to transform a wheelchair into the ADD. The wheelchair should be then very rigid, and at the same time adjustable, to make the isometric force measurements on three fingers, the lower arm, the trunk, the fundament and the foot on both left and right sides and at all three ADL postures. A wheelchair satisfying all these requirements would be so complex that patient entry and exit may well be impossible. If the wheelchair itself is not the ADD, the problem of transferring the patient from the wheelchair to the ADD must be solved. Considering the six ADL tasks already defined, the ADD must be equipped with instruments at the side, and in front of the patient. This makes a conventional tilting technique from a wheelchair to the ADD unadvisable. A survey of commercially available wheelchairs has shown that special

standard wheelchairs exist with some features that can make the transfer to the ADD very straightforward.

The third set of the criteria is concerned with the functional requirements of the units of the ADD. The functional requirements describe how the isometric forces and torques of the hand, the finger, the trunk, the fundament, and the foot should be measured with the selected commercial 6 DOF FT sensors.

The latest concept of the ALLADIN Diagnostic Device addresses all three requirement groups. The concept was modelled in the Pro/Engineer CAD system for the delineation of the proposed solutions.

1.4.2.4.1 Upper extremities

1.4.2.4.1.1 The finger device

Definition of grasping during the tasks

Task 1: Closure of the fingers (cylindrical grasp) with flexion of the wrist. The hand must be in close vicinity to the handle. The arm is beside the body.

Task 2: This is a typical cylindrical grasp but, with a slight extension of the wrist. The start positions for 1 and 2 are exactly the same, but the direction of expected forces and torques are different. No obvious wrist flexion is expected in task 2 (for normal people). Therefore strong flexion is a possible indicator for the level of recovery.

Task 3: The hand and fingers can start in the same position as above but the expected movement is extension of the wrist, ulnar deviation, internal rotation and an opening and slight spread of the fingers.

Task 4: Again, the same start position. As previously stated, the key should be oriented horizontally in the lock. Therefore lateral prehension and external rotation is expected, under normal circumstances.

Task 5: Reaching for the bottle is perhaps misleading. The bottle is placed out of the ‘hand grip’ to induce a preshape for grasping (finger extension). Aside from a different arm position, the hand position is the same.

Task 6: This is a pure grasping position of the fingers around the object.

Measuring positions for fingers are presented in Figure 44, Figure 45 and Figure 46.

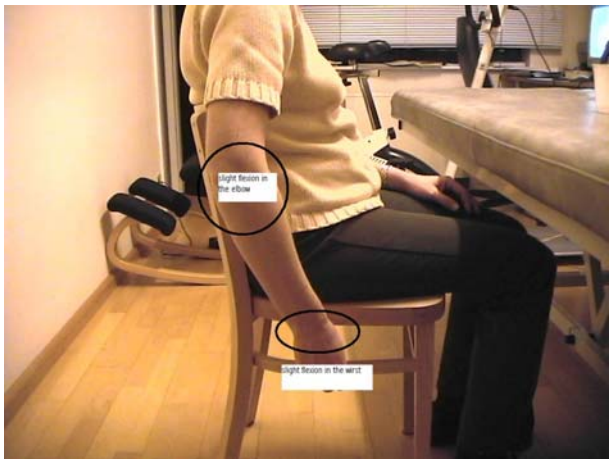


Figure 44 Position 1

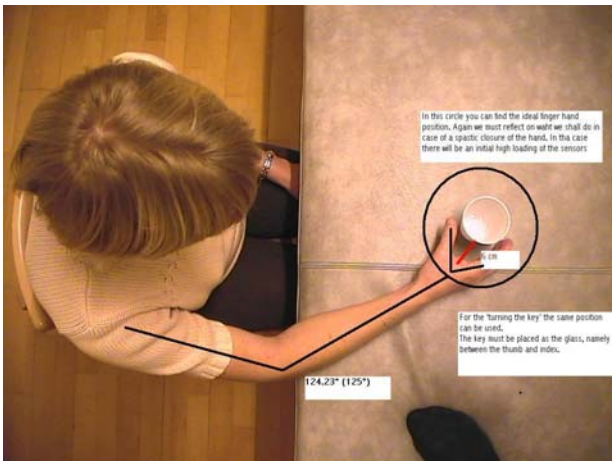


Figure 45 Position 2

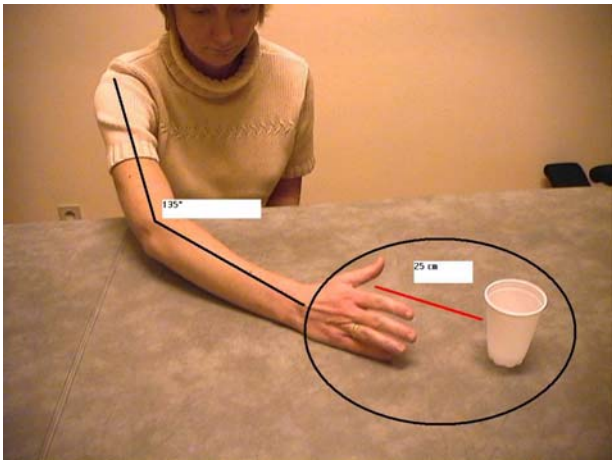


Figure 46 Position 3

Decisions

In connection with the finger device set-up the medical and engineering partner of ALLADIN decided that -

- Three sensors are required.
- 6D measurements for every finger are required.
- The arrangement should be: thumb #1, index finger #2 and middle finger at #3. The other two fingers are excluded from the measurement.
- The shape of the grasp should have the diameter of the glass (task2), in the range of 5 cm. The 'normal glass' is often inverse conical in shape. The other objects will be a spoon and a key. The start position for the hand is the same. For the key it will be a closure of the fingers and turning of the wrist combination. For the spoon a reaching to and opening of the fingers combination. The spoon will be placed slightly higher than the hand. This is necessary to induce an upward reach. A spoon lower than the hand cannot be isometrically simulated since there is eccentric muscle activity.
- The starting position of the fingers for the spoon and key is similar to that for the glass (position 2).
- The same finger measurement arrangement (and grasping device) is always maintained in positions 1, 2 and 3.
- The wrist will be linked to the lower arm.

The measurement setup for fingers, the solution

1st concept:

The first concept of the ALLADIN finger device has all three sensors located inside a box of approximately 130x65x100mm. The sensors would be enclosed within the housing and not visible to the patient. The configuration of the sensors allows measurements of the left or right hand by simply changing the orientation of the device (180 deg turn). Exchangeable finger fixations would be attached to the bars leading from the housing. Each finger fixation would be adjusted to the particular finger. The device could be mounted in any orientation or position allowing the measurement in the selected positions of the measurement protocol ("position 1", etc.).

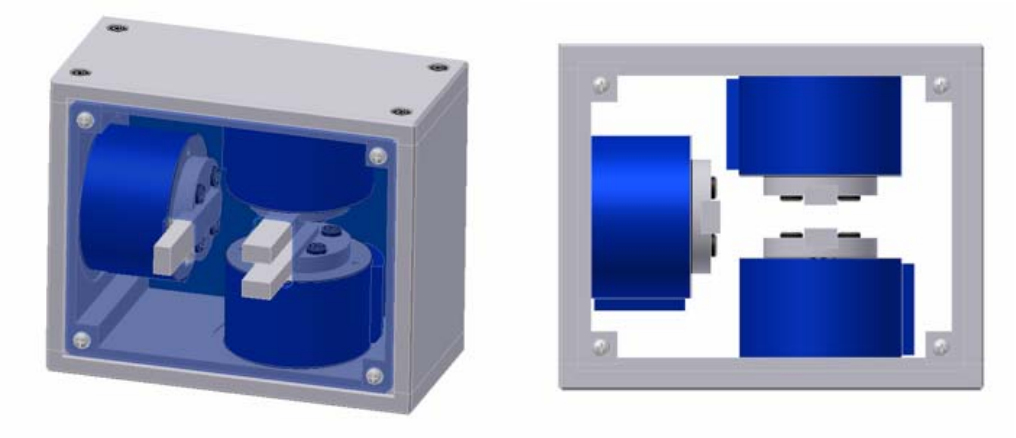


Figure 47 The first concept of the ALLADIN finger device with "internal" sensors.

2nd concept:

The second concept of the ALLADIN finger device has the sensors located on the outer side of the hand. The size of the device is about 220x100x170mm. The hand would be positioned between the two sensors for the fingers and the sensor for the thumb. The design of the device allows measurements for different hand aperture by adjusting the distance between the two sets of sensors (*red arrows*). The position of the device can be adjusted relative to the hand (*blue arrows*) in predefined discrete positions by adjusting the fixation knobs. Exchangeable finger fixations would be used to fixate the fingers and thumb in the correct position and allow transfer of forces & torques to the sensors. The configuration of the sensors allows measurement of the left or right hand by simply rotating the device through 180 degrees around a vertical axis. This design allows measurements with the object inserted between or close to the fingers.

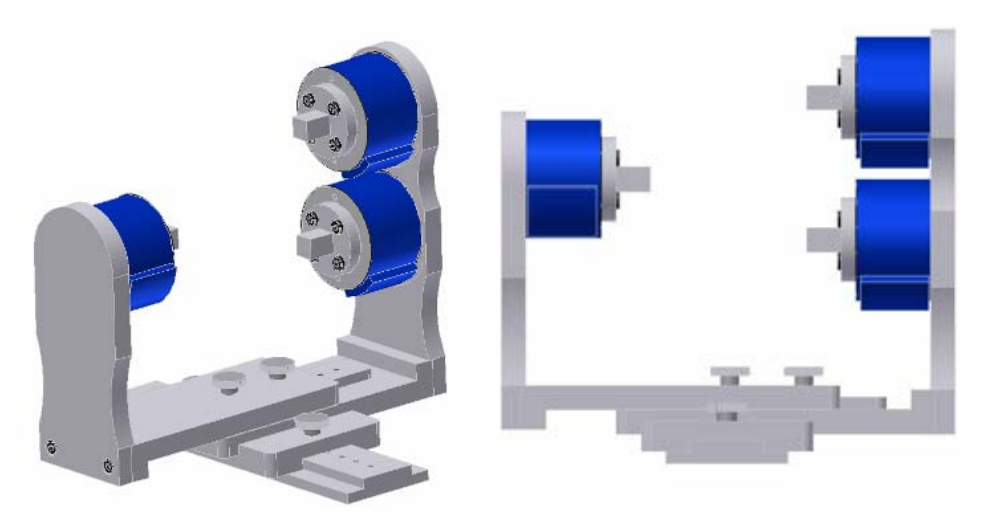


Figure 48 The second concept of the ALLADIN finger device with "external" sensors.

The fixation of the fingers

Different exchangeable finger fasteners will be used to fix the fingers in the correct starting position. Each finger fastener is fitted to a particular finger.

The fingers will be strapped to the fixations using a Velcro-type strip to prevent movement in either direction (Figure 49). Such a configuration would allow the measurement of forces and torques during, for example, opening or closing of the hand.

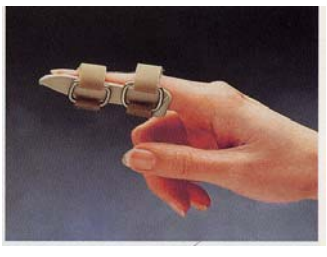


Figure 49 Fixation of finger

1.4.2.4.1.2 The arm device

Given the conclusions of the anthropometrical design, a single, fixed, and flat table cannot be used for all patient sizes. The table, on which real objects are presented to the patient, will be moved with the arm device. To reduce the weight of the arm device the table will be manufactured from light weight material and, be as small as possible.

The lower arm orthosis is integrated with a functional table (shown in Figure 50), on which is placed the real objects of the selected ADL task (except ADL1):

- spoon
- glass
- bottle
- key

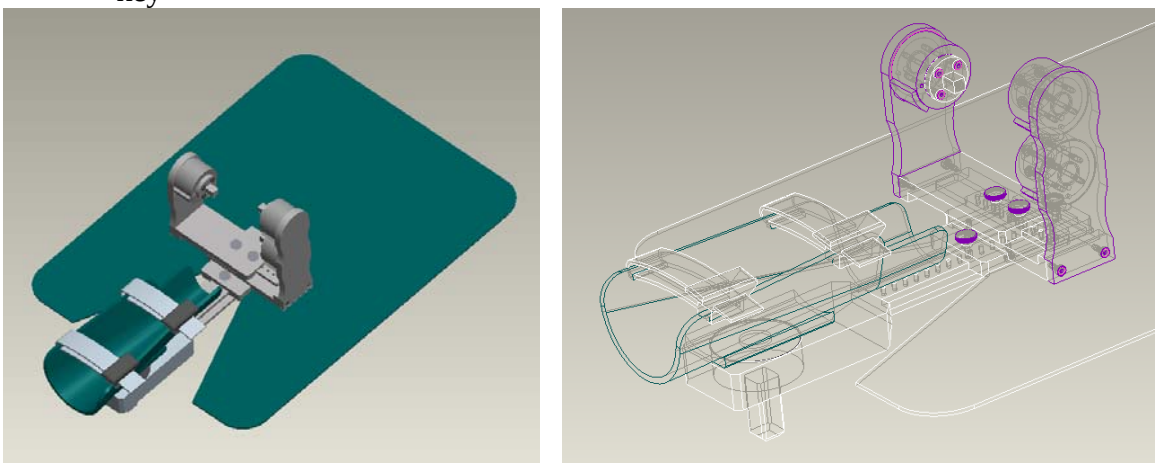


Figure 50. Structure of the lower arm orthosis and the finger device

The current version of the arm device is a narrowing half tube splint with two Velcro fixations at the front and rear of the lower arm. The splint size and the polyurethane foam lining inside will be such that a single splint will fit all patients. The front part of the splint is shaped to support the wrist and palm. The lower arm is fixed in a position determined by the finger position in the finger device.
In other words we aim to design an arm orthosis suitable for all patients. The 6 DOF FT sensor is located under the orthosis. The finger device is fully integrated with the arm device through the socket of the arm 6 DOF FT sensor.

The arm device together with the finger device will be positioned in each of the ADL positions according to whether the patient is small, medium or large (S, M, L). To position properly the physiotherapist must move the total weight of the arm device, the finger device, and the patient's arm. A very simple mechanical plug (Figure 51) will be positioned on the bottom of the arm device. The physiotherapist then need only remove the plug from its socket and plug it into the next socket in the sequence Pos1 to Pos2, and Pos2 to Pos3.

Figure 51. Standard plug and socket used for fixing wheelchair arm rest

1.4.2.4.2 Trunk

Stroke patients often compensate trunk movements for arm movements. To accurately determine the full extent of this compensation we must measure the isometric forces at both the arm and trunk.

The trunk device is shown in position 3 in Figure 52. A detachable wedge is proposed to fix the patient's 'twisted' posture in position 3. The physiotherapist will insert a left or right sided wedge, depending on the patient's affected side, when he/she moves the patient from Pos2 to Pos3. The trunk device can be positioned for measurements by pulling it down on a vertical guideway. To reduce the physiotherapist's workload a weight counterbalancing mechanism will be used. The spring shown in Figure 52 is a symbolic representation of the counterbalancing mechanism. 'End stops' will be located on the vertical guideways to allow an accurate and reproducible positioning of the trunk device. The trunk device, similarly to the device used during the preliminary isometric force measurements, will have a sandwich structure. The X-ray picture (Figure 53) of the trunk device shows the 6 DOF FT sensor between the two plates.

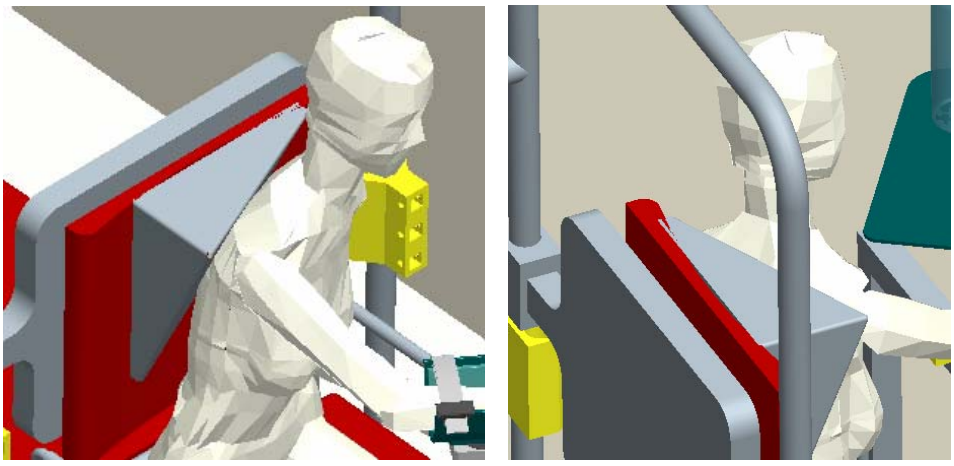


Figure 52. 25%-ile female in Pos3 ADL5 rear view.

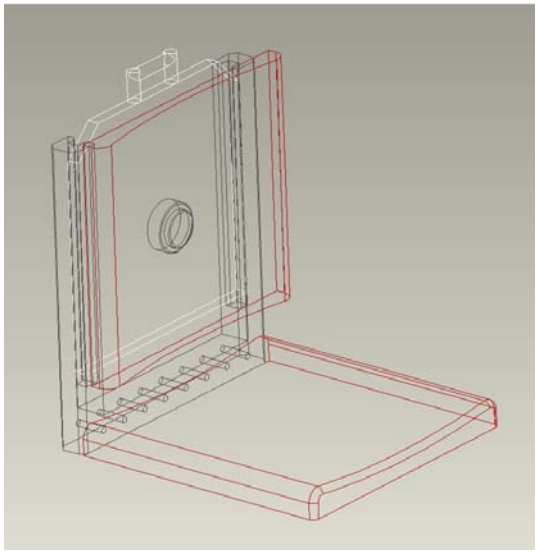


Figure 53. The sandwich structure of the trunk device

The patient will be fixed to the trunk device using a standard wheelchair belt (Figure 54).

Figure 54. Standard wheelchair belt

1.4.2.4.3 Fundament

For good functional performance of the activities of daily living an individual should be able to sit symmetrically in a chair. Rehabilitation of stroke patients must therefore facilitate relearning this symmetry. At the seat level, functional weight bearing during different ADL tasks will be measured and analysed.

The fundament device of the ADD includes a rigid seat plate assembled on a lever (Figure 55). There is a high load capacity 6 DOF FT sensor between the lever and the seat plate. Before the patient comes to the ADD the fundament device shall be lowered and the width adjusted for S, M, L patient sizes. During docking of the wheelchair the fundament device can slide into the space between the cross links and the linen seat of

the wheelchair. This space is indicated with a triangle in Figure 56. The physiotherapist must lift the fundament device by approximately 30 mm, which is well below the maximum deformation of the linen seat of the wheelchair. Figure 55 shows a simple mechanical device, a crank mechanism that requires only a half turn rotation of the crank lever to produce 30 mm elevation at the end of the seat lever. The final ADD may include an even simpler mechanism. When the patient is lifted the PT can detach the already flexed linen seat of the wheelchair from the frame of the wheelchair. You can see that the excess sides of the linen seat fold down on the fundament device.

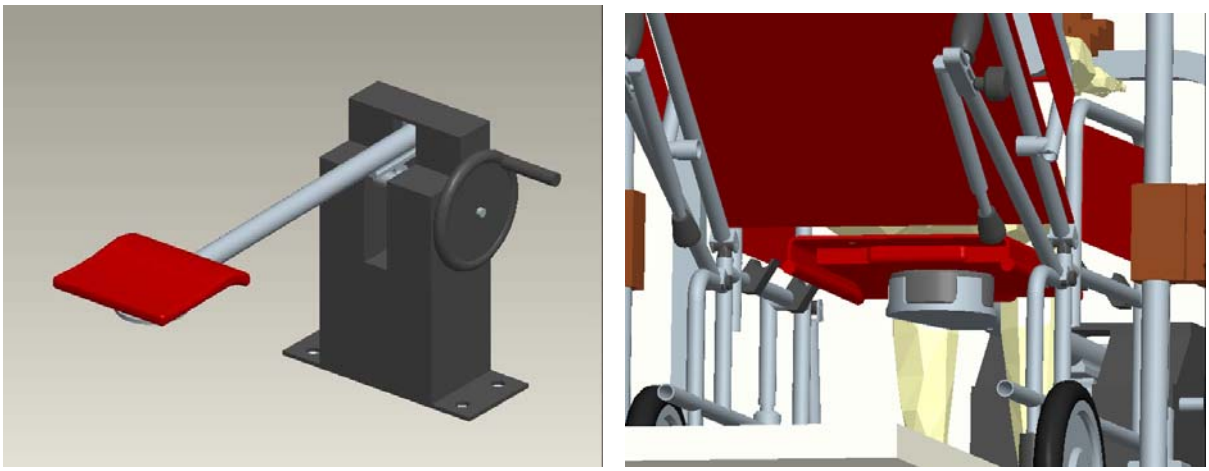


Figure 55. Provisional lifting mechanism of the patient (left) and the location of the sensor measuring the forces and torques of the lower trunk at the patient's fundament (right)

Figure 56. The space for the fundament device under the seat of the B4205 transit lying wheelchair

1.4.2.4.4 Lower extremities

The aim of the investigation carried out by SSSA so far was to define several possible concepts of the measurement system to record FT information from the foot and the big toe during isometric contractions.

During the first part of the work, different concepts were realized addressing also the problem of the definition of the biomechanical constraints to be imposed on the lower extremity of the patient while recording (in particular for the Position2 defined by the clinical partners, see Figure 57).

Figure 57 The two different starting positions for the lower extremities and the feet for the different ADLs selected. Position 1 (left), Position 2 (right).

Figure 58 shows three different possible static postures for Position2.

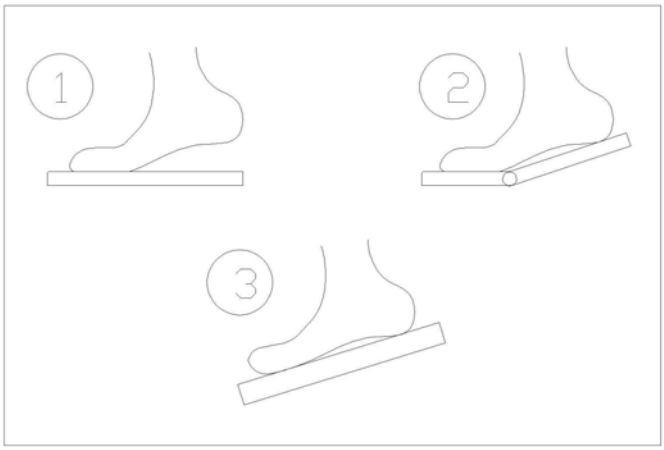


Figure 58 Three different structures of the device for Position2

Figure 59 shows different concepts designed according to postures 2 and 3.

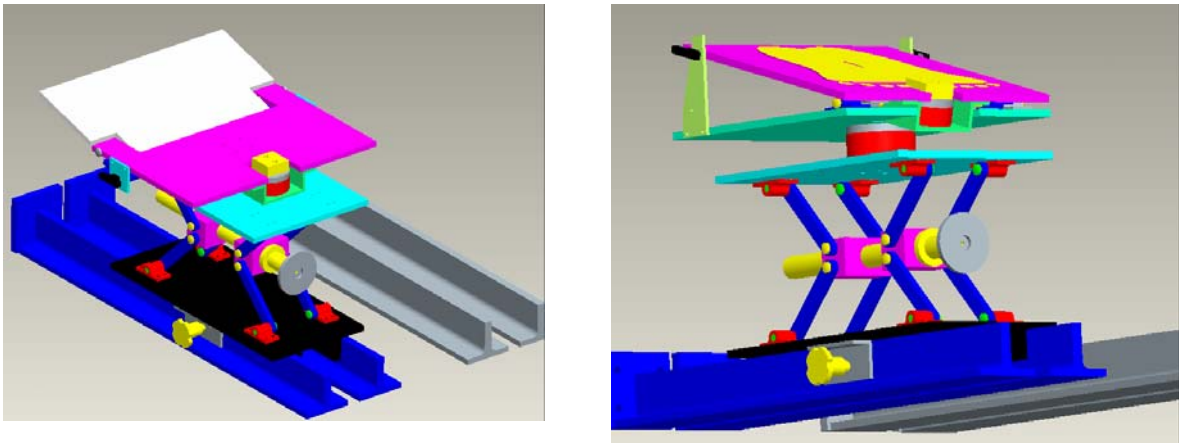


Figure 59 Concepts designed during the first phase of the project for solutions 2 and 3 for Position2

After an internal “brainstorming” phase with the other partners of the ALLADIN Consortium, solution 1 of Figure 58 was selected. Therefore, the following concept (henceforth named as ADD_FBT_v1) was identified for the "foot-big-toe" device (see Figure 60 showing the device from different angles):

- Two tracks are connected to the ADD using screws;
- The basement slides on the tracks and it is blocked through two pins in the corresponding hole;
- 4 holes on the top row refer to mannequin (i) 95 percentile man, (ii) 50 percentile man, (iii) 50 percentile woman, (iv) 25 percentile woman, for position 1 and position 2. The 5 percentile woman was not added yet but it can be easily done later;
- 4 holes in the bottom row refer to the same percentile of top row, for position 3;
- The PT can adjust the height of the device by using the 4 holes of the single support, related to the different percentiles. A mechanism to speed-up the operation is foreseen:
  - a counterbalancing mechanism
  - a lever mechanism
  - a system with clicks which allows to lift the platform just using a handle (10-15 mm for each click)
- The PT positions the sensorised platform (made to slide on the track) on the affected side of the patient. He/she blocks it through the double pin and inserts the non-sensorised platform in the four-holes.

The sensorised platform is symmetric: the sensors for both the foot and the big toe are positioned in the centre of the platform to allow measurements on both feet.

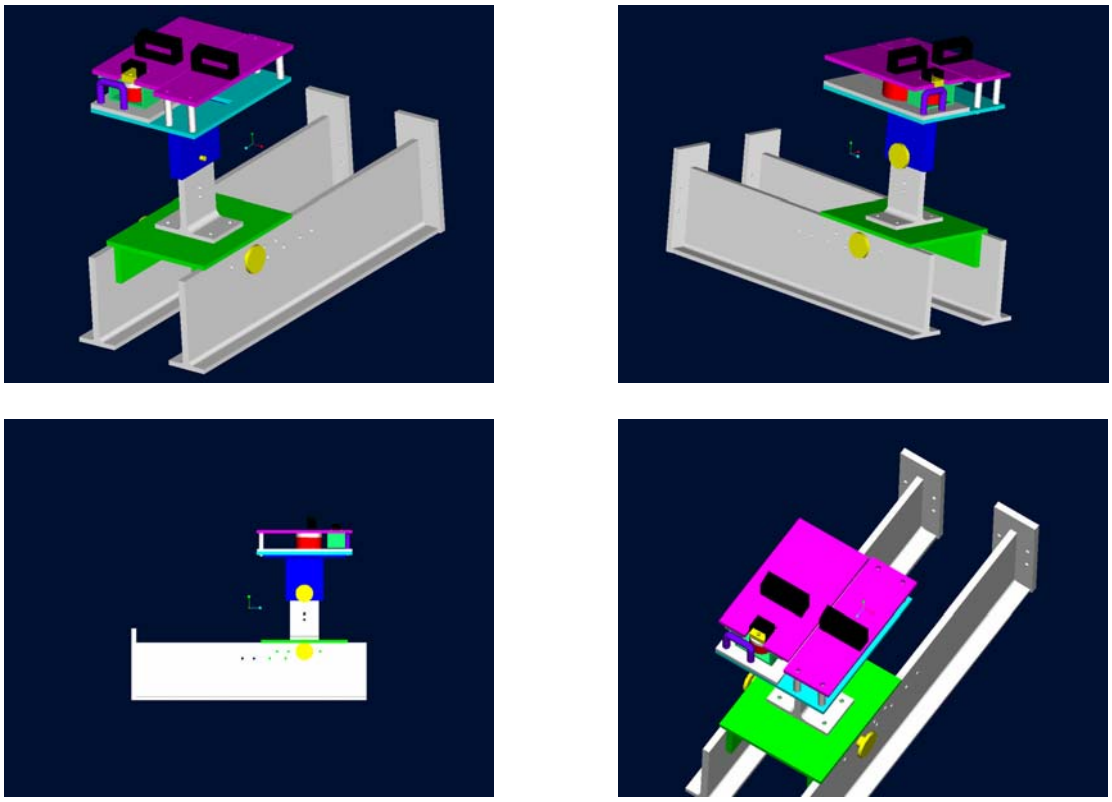


Figure 60 Different views of the ADD_FBT_v1

Figure 61 shows the ADD_FBT_v1 for position 1 (left) and position 2 (right) with 25 percentile female mannequin.

Figure 61 Concept ADD_FBT_v1 for position 1 (left) and position 2 (right) with 25 percentile female mannequin.

Other ideas have been proposed, for example using a skidding mechanism (Figure 62). An additional track to reach position2 from position1 is not drawn in the following figures.

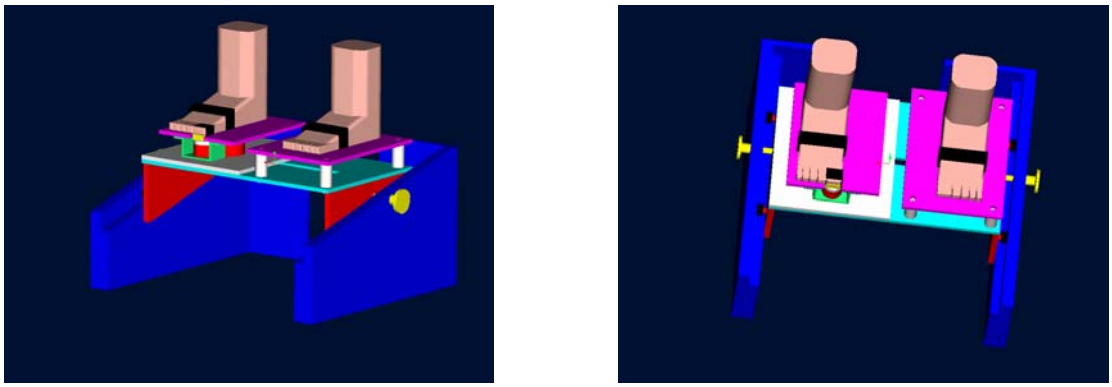


Figure 62 Concept ADD_FBT_v1 using a skidding mechanism

Finally, it is important to point out that the above mentioned are preliminary concepts which will be finalized in the near future according to the feedback of the ALLADIN Consortium.

1.4.2.5. The concept of the ALLADIN Diagnostic Device

1.4.2.5.1 Problems associated with the anthropometric constraints

The conceptual design of the ALLADIN Diagnostic Device is illustrated in this section using an extensive set of pictures. Problems associated with the anthropometric constraint are demonstrated.

Figure 63 presents the finger matching problem and the serious collision problem arising at the lower arm in case of the 5%-ile female and the 95%-ile male subjects, respectively. The left picture shows the arm device set to the S hole of the Pos2 arm fixture, whilst in the right picture the arm device is set to the L hole of the Pos2 arm fixture. The finger device shown is not the latest version but it demonstrates the need for an S-M-L setting for the final finger device. The three real objects: the glass, the key, and the spoon (fork is shown) will be placed on the table one after another, so all three objects will never be on the table together.

Collisions will not of course happen in reality. Collisions between the arm and orthosis shell are shown as intersections between the arm and the orthosis. Collision and setting problems due to the anatomical differences of the patients are also shown in Figure 64 and in Figure 65 .In reality, the patients who do not perfectly fit the S, M, and L settings will be accommodated with errors in the anatomical angles. A detailed reliability study will reveal the anatomical angle errors.

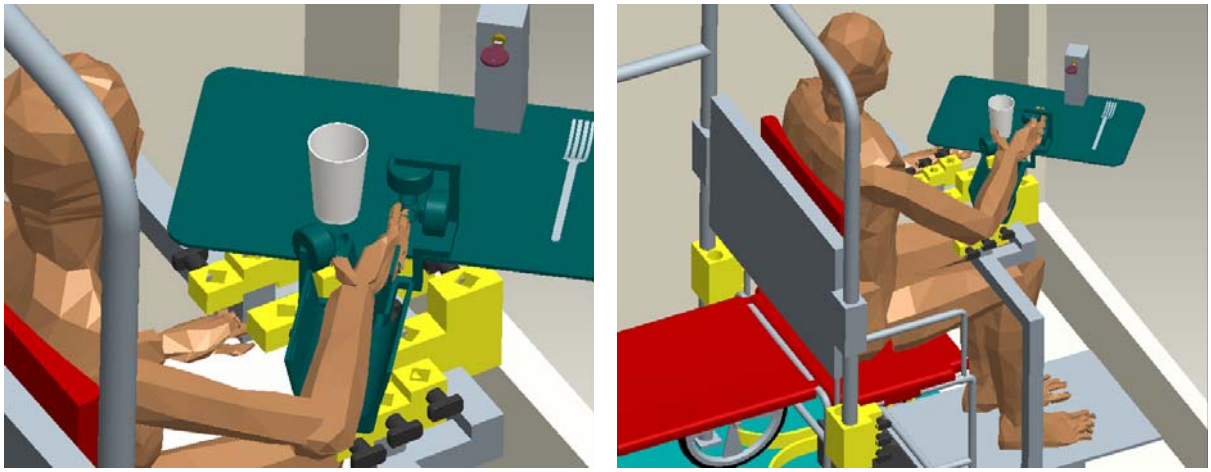


Figure 63. 5%-ile female in Pos2 ADL2: finger matching problem (left), 95%-ile male in Pos2 ADL2: serious collision problems at the arm and fingers (right)

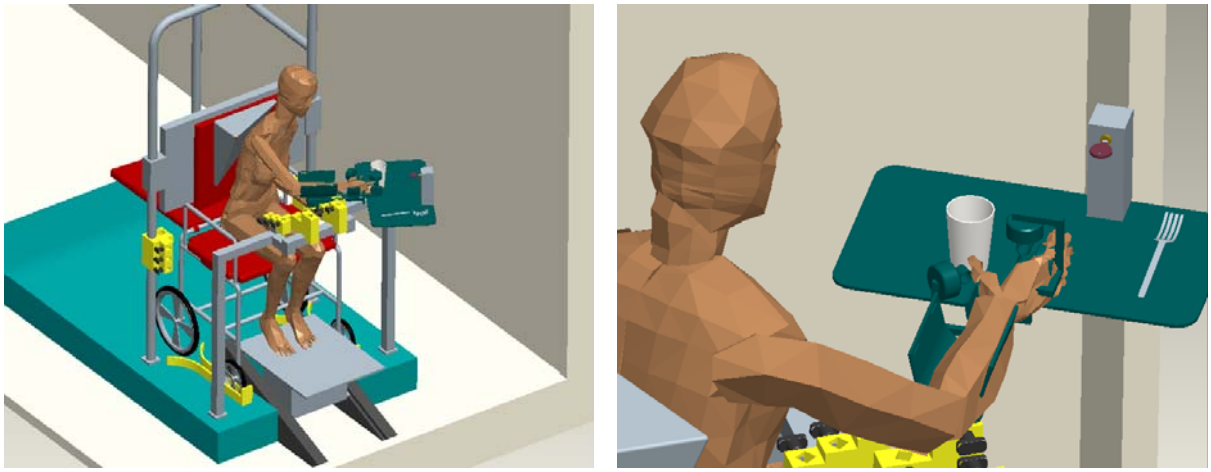


Figure 64. 5%-ile female in Pos3 ADL5: no contact between the back rest and the back (left), 95%-ile male in Pos3 ADL5: serious collision problems at the arm and fingers (right)

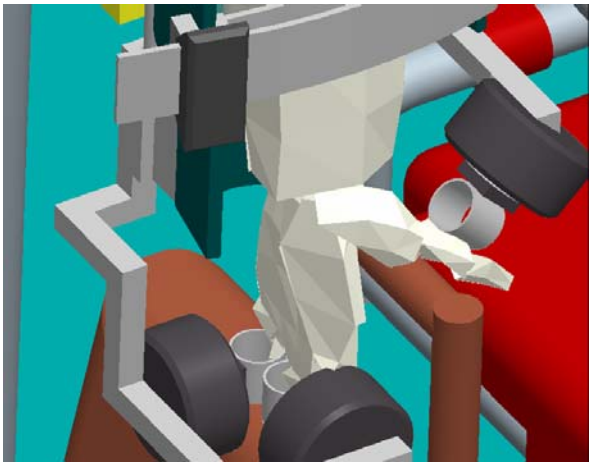


Figure 65 25%-ile female in Pos1 ADL1: her thumb does not fit the finger device (left), 25 %-ile female in Pos2 ADL3: fingers matching problem (right)

1.4.2.5.2 The integrated ADD

The following pictures illustrate the first concept of the ADD. The integrated ADD is shown in the three different positions of the selected ADL task. The foot, fundament, trunk, arm, and finger devices designed by BUTE, SSSA and ULFE are included in the model.

1.4.2.5.2.1 ADD set to Position 1

Figure 66 shows the patient in ADL1 Pos1. The patient sits on the fundament device. The trunk device is pulled down and positioned. The patient is fixed to the trunk device by a wheelchair belt. The arm and finger devices are positioned on his right arm, and set to the Pos1 fixture. The patient can hold his arm at the side of his body, since the width of the fundament device is adjusted to his size. This results in a normal (low) shoulder abduction angle. The brown fixtures have three rectangular holes for the 25%, the 50%, and the 75% settings of the arm-finger device. The bag support also has three different settings to allow the patient's fingers to be in constant contact with the handle of the bag. The right foot and the right toe do not precisely fit the foot device. This is due to the incorrect estimation of the anthropometrical requirements at this conceptual design stage. The patient watches the monitor (which cannot be seen because of the wall) which shows the video demonstration of ADL1.

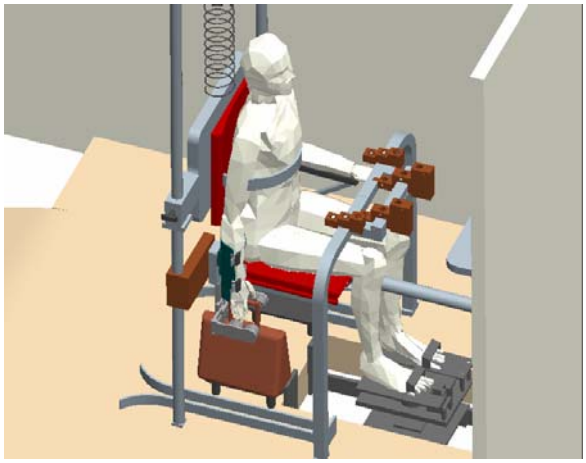


Figure 66 The 50%-ile male is measured in Pos1, ADL1

1.4.2.5.2.2 ADD set to Position 2

Position 2 of the ADD covers three ADL tasks: No. 2 grasping a glass, No. 3 reaching for a key to turn it, and No. 4 reaching for a spoon to grasp it. Figure 67 shows the ADD set to ADL2. The patient sits on the fundament device, and leans against the back device. The arm and finger devices are placed to the fixture in front of the patient. The glass is placed close to the patient's fingers and the patient has a good view of the real objects. The finger device does not include the finger fixations which will need to be considered in the final design of the ADD. The foot remains in the same position as in Pos1. Figure 68 left shows the ADL3 object: a lock with a horizontally oriented blade. Horizontal orientation is important to maintain the same

starting posture for the hand as in ADL2. Figure 68 right shows the last ADL in this position: ADL4 reaching a spoon. The spoon will always be positioned on the external side of the hand, i.e. in the case of a right hand exercise the spoon is located on the right side of the arm. It is important to place the spoon on a small box in order to induce a small upwards motion. Also in ADL4 we can maintain the same starting posture of the hand as in ADL2, and ADL3. Since the fingers of the S, M, and L patients change their location relative to the table, footprints will indicate the correct S, M, and L positions of the real objects.

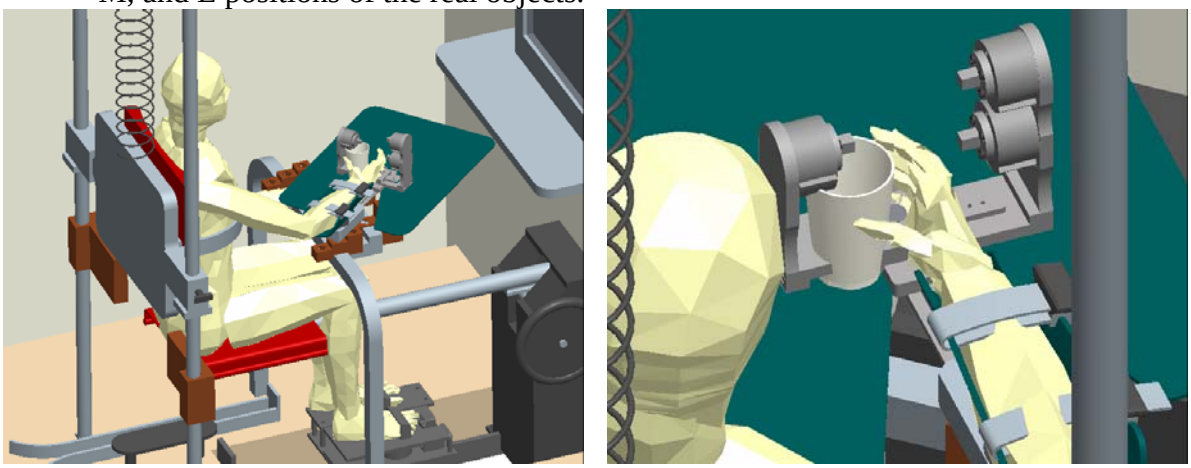


Figure 67. 50%-ile male in Pos2 ADL2

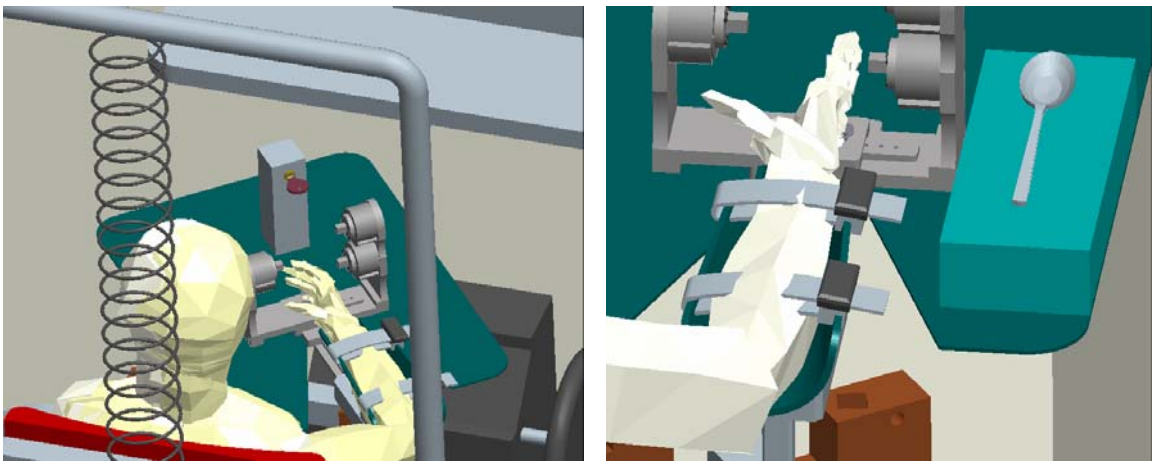


Figure 68. 50%-ile male in Pos2 ADL3 (left) and ADL4 (right)

1.4.2.5.2.3 ADD set to Position 3

Pos3 radically differs from Pos1 and Pos2. In position 3 the patient's trunk leans forward and is twisted towards the non-affected side. In order to allow the patient to reach as far forward as possible the foot will also slide back under the fundament device. To visualise this movement please refer to Figure 41. To move the patient from Pos2 to Pos3 the PT shall move the arm and finger device, the trunk device and the foot device. In the case of the trunk device, an upholstered right or left sided wedge should be inserted between the patient's back and the trunk device. Before so doing, the patient's wheelchair belt will be loosened and the patient will be leaned forward. The wedge will also have a fixture so the PT can easily fit it in place. After

wedge insertion, the patient's wheelchair belt will be tightened. The foot device will also be pushed back on the horizontal guideway until the relevant S, M, or L spring bolt locks it. The patient's heel will elevate automatically to a natural position. In ADL5 the patient will reach for a bottle (Figure 69). In ADL6 the bottle is placed close to the fingers and should be moved to another table coloured grey in Figure 70. The hand posture is the same in ADL5 and ADL6 as in previous cases, so the hand posture is fixed for all ADLs. The correct position of the bottle will be indicated by footprints on the table and denoted by S, M, and L markings.

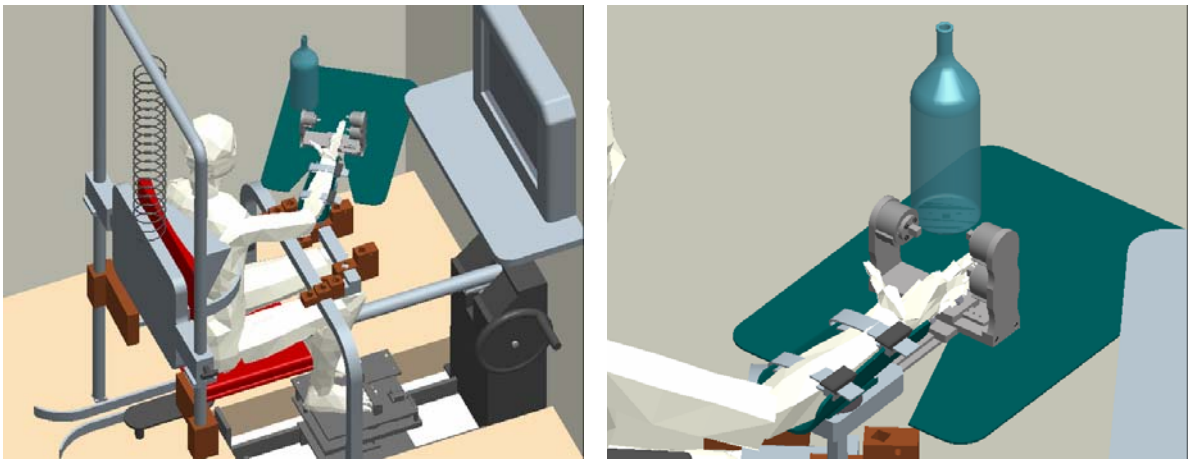


Figure 69. 50% male in Pos3 ADL5

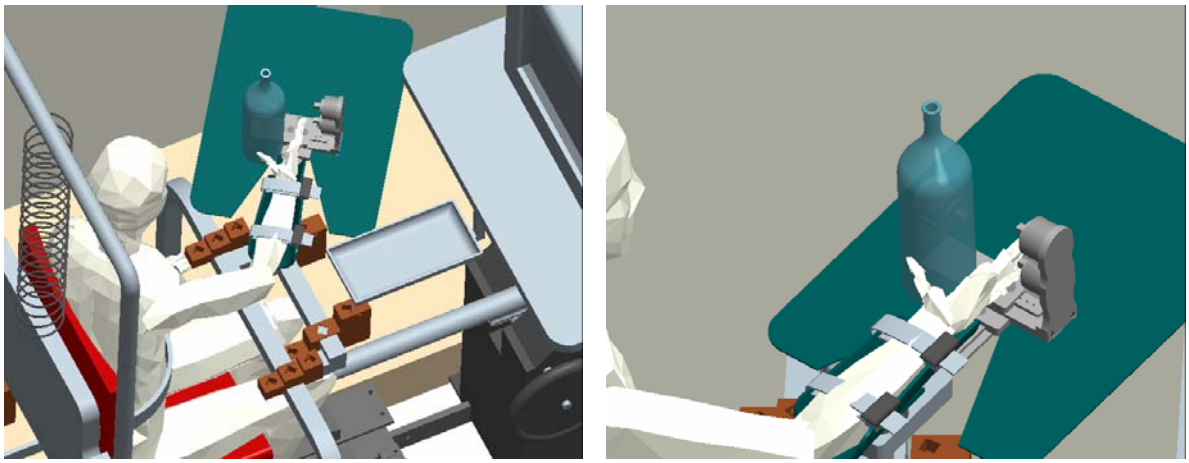


Figure 70. 50% male in Pos3 ADL6

1.4.2.5.3 Envisaged scenario

The full measuring cycle of the isometric FT measurements is divided into three sections. First, the patient will be moved to the ALLADIN Diagnostic Device by the physiotherapist. This is called "patient entry". This also includes the fixation of the patient to the trunk device and, the removal of the wheelchair which in turn makes patient handling as easy as possible for the physiotherapist. The next step is the measurement of isometric FT trajectories at the initiations of the selected ADL tasks. The six different ADL tasks are described in detail and in the correct order in section

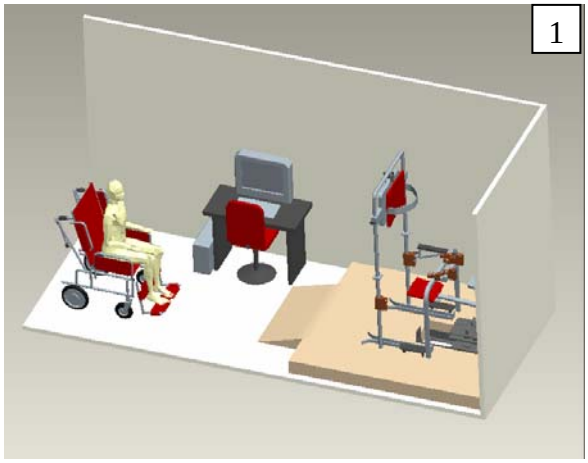
1.4.2.1.2. At the beginning of each measurement the patient is shown a video clip of the task to be completed and then invited to complete the task. Finally, the physiotherapist moves the patient out of the ALLADIN Diagnostic Device. This is called “patient exit” and is the reverse order of “patient entry”. In this way, at the end of the full measurement cycle, the patient is seated in the same wheelchair in which he/she arrived to the ALLADIN Diagnostic Device.

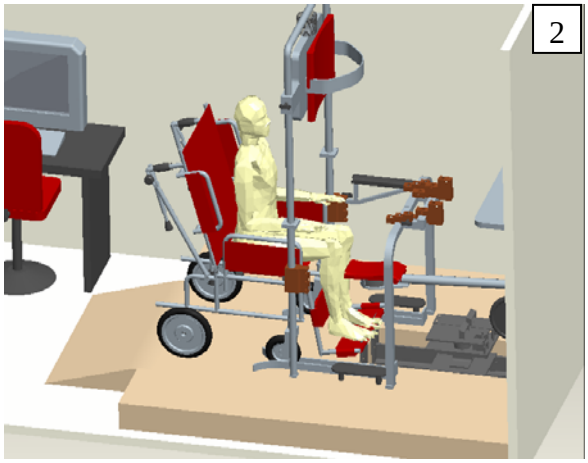
The envisaged scenarios of the above three different parts of the full measurement cycle are explained in detail in the following sections in which point-by-point explanations are also illustrated by serial pictures.

1.4.2.5.3.1 Patient entry to the ALLADIN Diagnostic Device

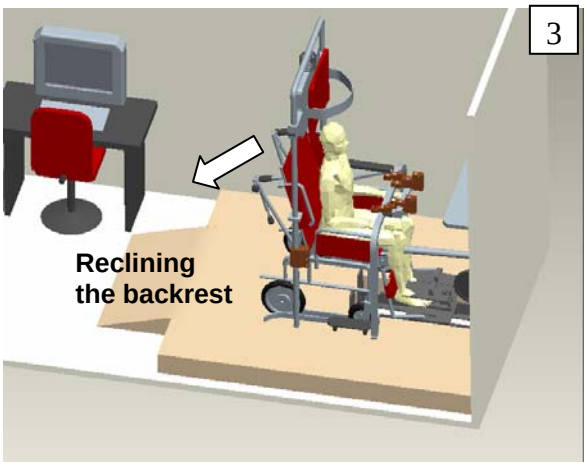
Envisaged scenario for the patient entering is as follows:

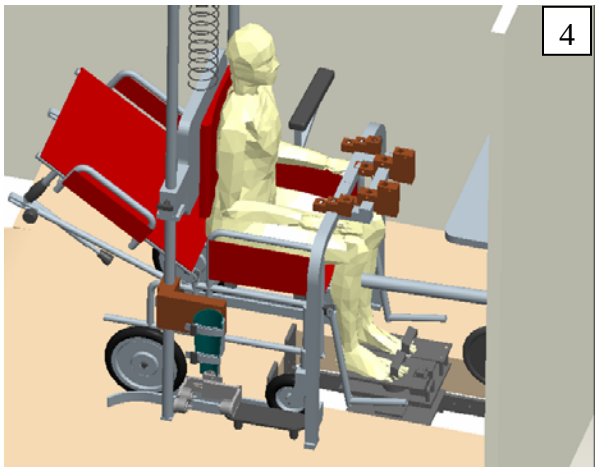
1. The patient is seated in the wheelchair outside the ADD.
2. The PT pushes the wheelchair to the ADD
3. The PT reclines the backrest of the wheelchair
4. The PT fixes the patient to the instrumented backrest
5. The PT unfold the narrow seat device under the wheelchair seat
   (For the sake of visibility the patient and wheelchair are not shown in he picture)
6. The PT lifts the patient with the simple mechanical lifter
7. The PT positions the instrumented backrest
8. The PT disconnects the linen seat from the wheelchair
9. The PT removes the wheelchair from the system
10. The patient is sitting in the ADD

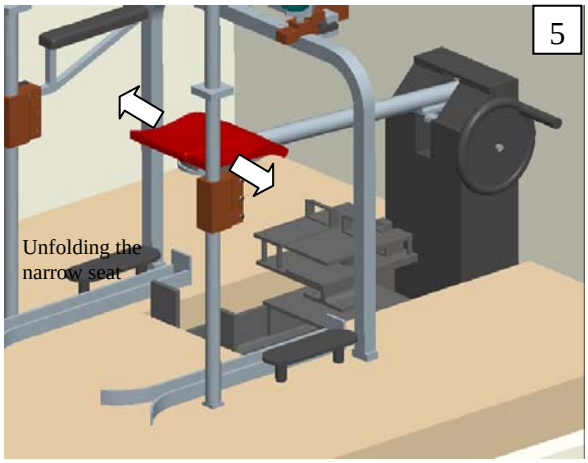


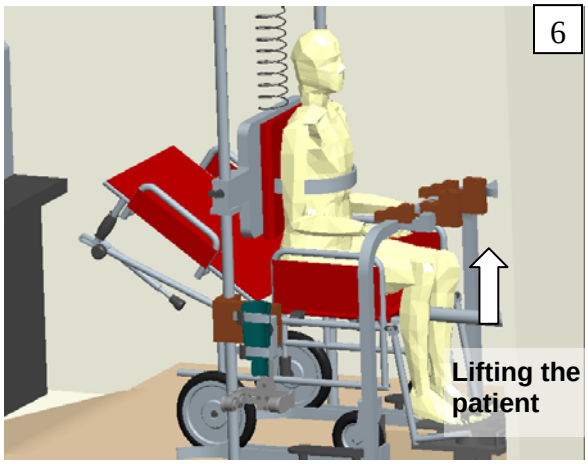


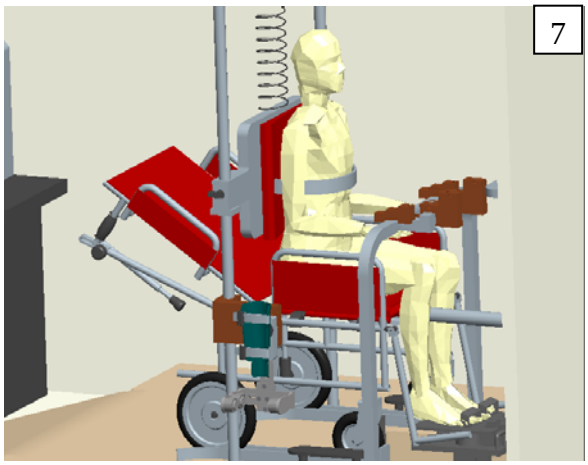
The total necessary time for starting the ADD software, patient entry including fixing the patient’s arm, foot and fingers to the lower arm orthosis and to the foot and finger devices respectively, and also, setting the ADD to Position 1 is approximately **300 seconds**.

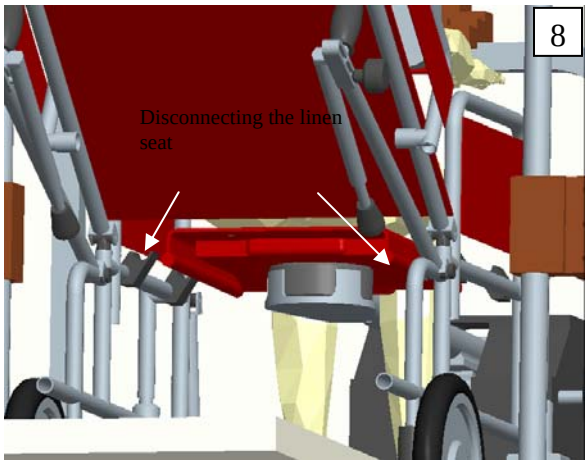

3
Reclining
the backrest

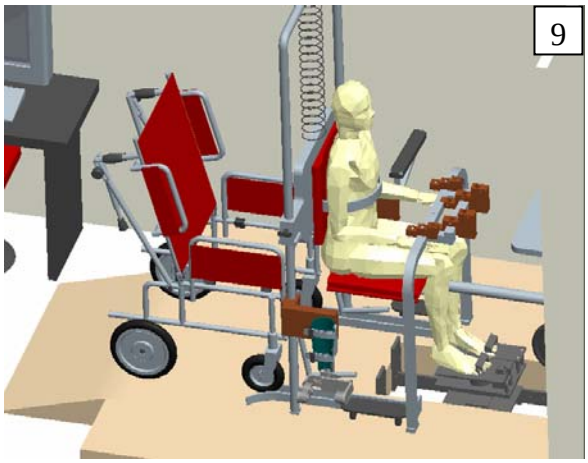

4

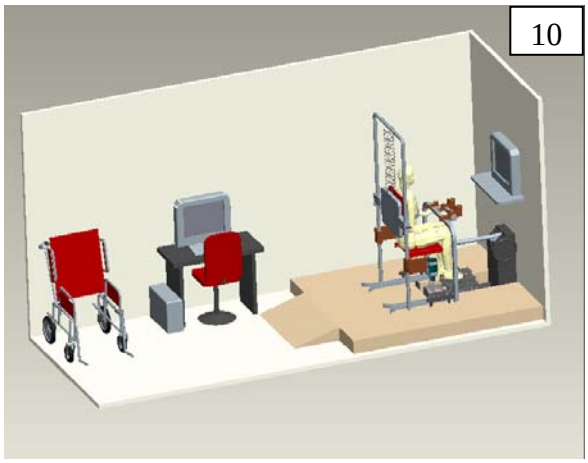

5
Unfolding the
narrow seat


6
Lifting the
patient


7


8
Disconnecting the linen
seat





Note: In the second step, when the physiotherapist pushes the wheelchair to the ADD where a guiding and locating system will be used to make wheelchair maneuver easier. wheelchair. This system also ensures that the patient will be seated in the same position for every measurement session in the ADD. As the vertical stroke of the lifter is only 40 mm, lifting will not be tiresome for the physiotherapist.

At the conclusion of “patient entry” the patient is sitting in the ADD device and the experiment can be started.

1.4.2.5.3.2 Isometric FT measurements of the selected ADL tasks

Envisaged scenario for isometric FT measurements of the selected ADL tasks is:

11. The PT measurement of ADL1 (ADD is already set to Position 1)
12. The PT resets the ADD to Position 2 and measures ADL2
13. The PT changes the object and measures ADL3
14. The PT changes the object and measures ADL4
15. The PT resets the ADD to Position 3 and measures ADL5
16. The PT changes the object and measures ADL6

The isometric FT measurements of a particular ADL task include the following steps:

1. Video presentation of the particular ADL task
2. Patient memorising of the particular ADL task. (The task is demonstrated in a video clip as shown in Figure 71) The final video demonstration will include a clip shot on an exercise done in the real ADD.

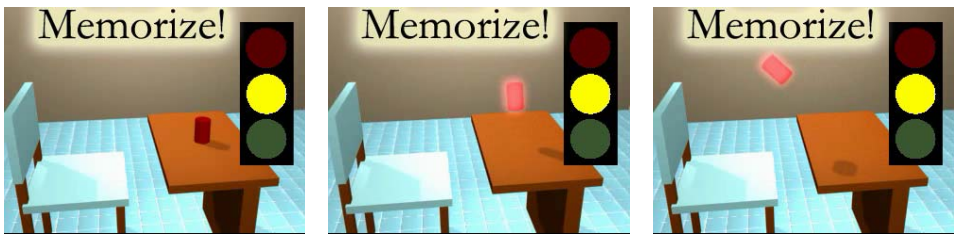
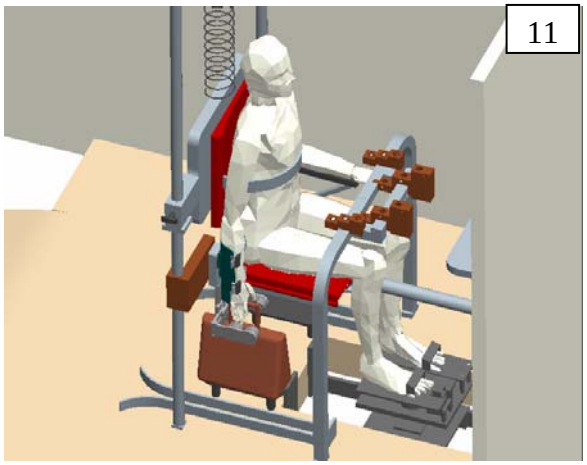
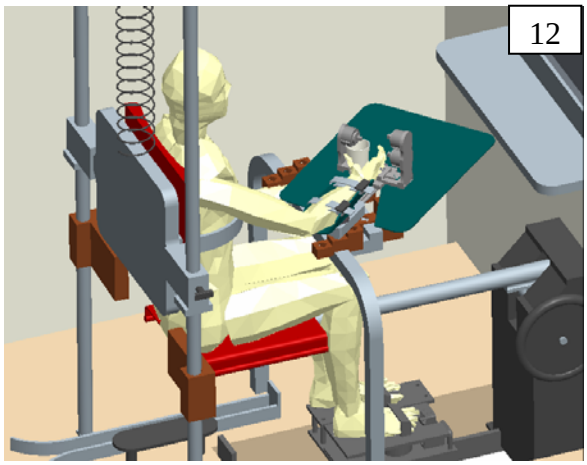
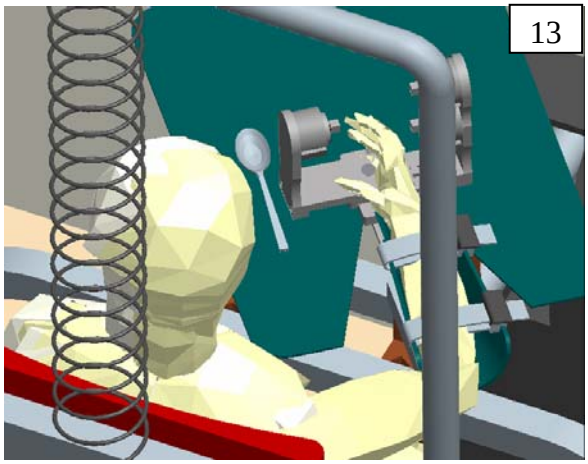


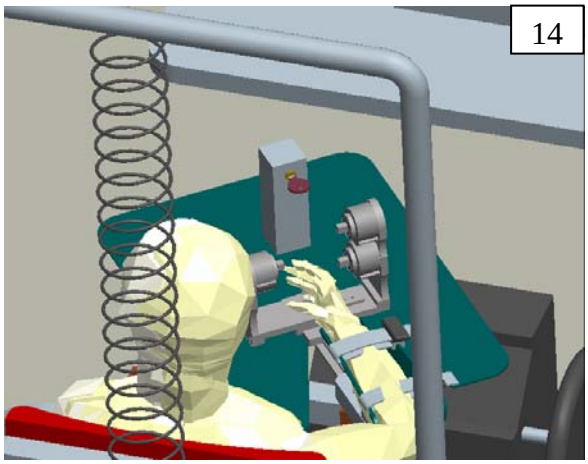
Figure 71 Video demonstration of ADL2 (drinking a glass of water)

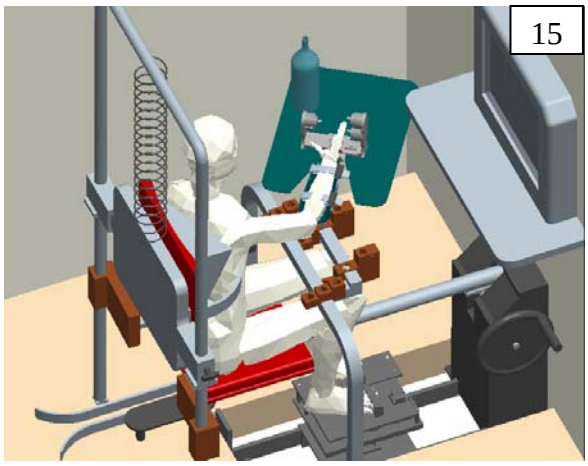
3. The patient initiates the particular ADL task for the first time
4. The patient is allowed to rest
5. The patient initiates the particular ADL task for a second time
6. The patient is allowed to rest
7. The patient initiates the particular ADL task for a third time
8. The ADD is reset for the next task

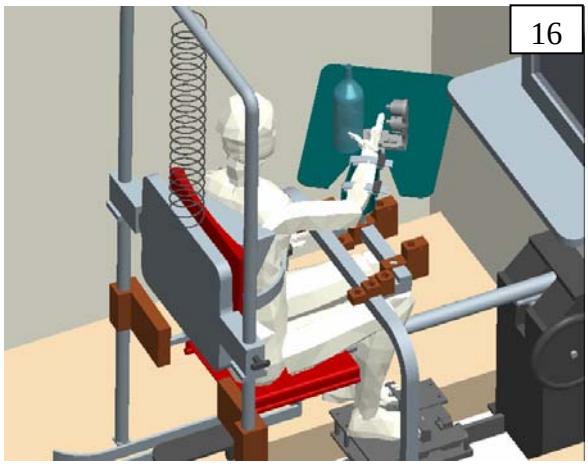








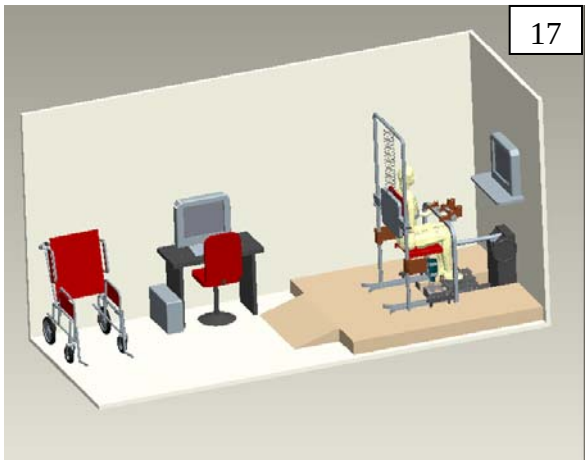


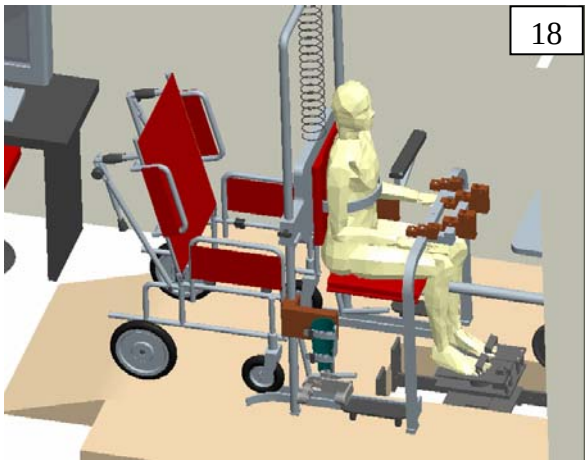


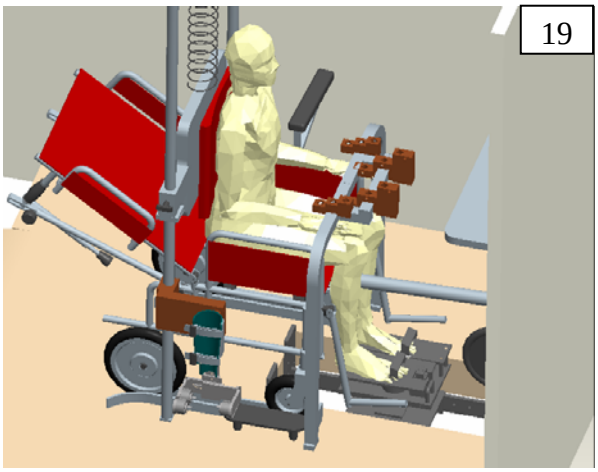
1.4.2.5.3.3 Patient exit from the ALLADIN diagnostic Device

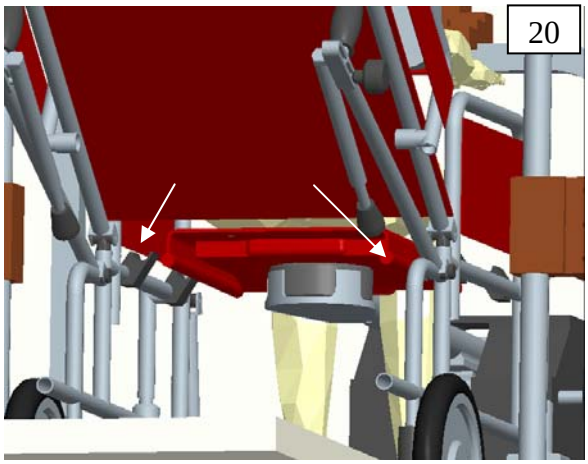
Envisaged scenario for moving the patient out of the ADD is as follows:

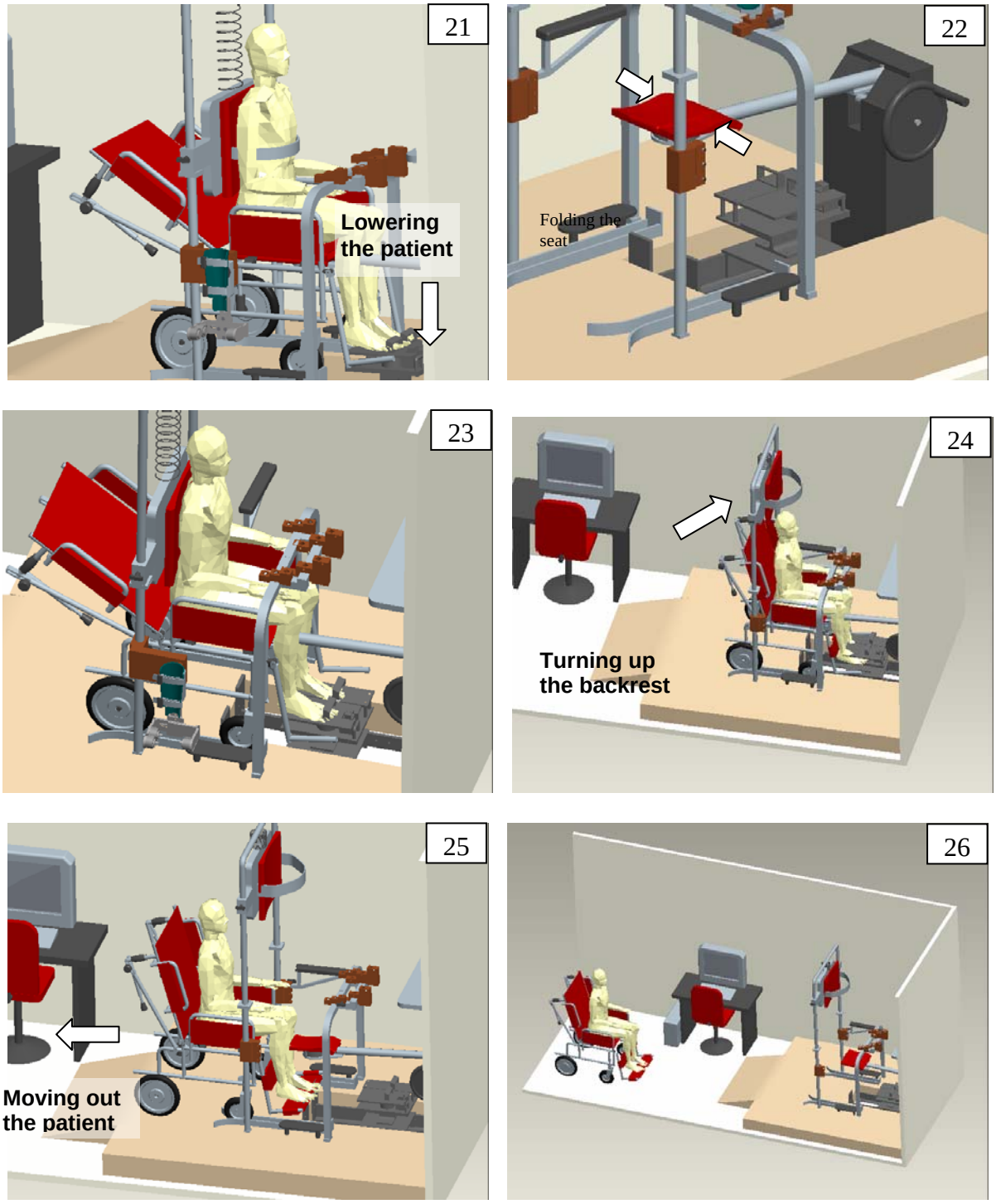
17. The patient is sitting in the ADD.
18. The PT pushes the wheelchair to the ADD
    (the backrest of the wheelchair must be reclined)
19. The PT unlocks the fixation on the instrumented backrest
20. The PT reconnects the linen seat to the wheelchair
21. The PT lowers the patient into the wheelchair
22. The PT folds the seat device under the wheelchair
23. The PT disconnects the patient from the instrumented backrest
24. The PT moves the backrest of the wheelchair up
25. The PT moves the patient out from the ADD
26. The full measurement cycle is ended and the patient is sitting in the wheelchair outside the ADD











The estimated time for the “patient exit” equals that for “patient entry”.

1.4.2.5.3.4 Cycle time study

To allow for the required patient turnover, a 30 minute net measuring time is allocated for the isometric force measurements. In this section we give the first estimate of the cycle time broken down to include all processes. The final cycle time of the isometric force torque measurements is 20 minutes according to Table 15.

Operation	Time [sec]
Patient entry, setting of the ADD to ADL1, start of the Measuring SW	300
Video presentation of ADL1	5
Memorizing	5
Exercising	2
Resting	20
Exercising	2
Resting	20
Exercising	2
Resetting of the ADD to ADL2	30
Video presentation of ADL2	5
Memorizing	5
Exercising	2
Resting	20
Exercising	2
Resting	20
Exercising	2
Resetting of the ADD to ADL3	5
Video presentation of ADL3	5
Memorizing	5
Exercising	2
Resting	20
Exercising	2
Resting	20
Exercising	2
Resetting of the ADD to ADL4	5
Video presentation of ADL4	5
Memorizing	5
Exercising	2
Resting	20
Exercising	2
Resting	20
Exercising	2
Resetting of the ADD to ADL5	180
Video presentation of ADL5	5
Memorizing	5
Exercising	2
Resting	20
Exercising	2
Resting	20
Exercising	2
Resetting of the ADD to ADL6	25
Video presentation of ADL6	5
Memorizing	5
Exercising	2
Resting	20
Exercising	2
Resting	20
Exercising	2
Patient exit	300
Total	**1181**

Table 15 Cycle time summary of one isometric force measurement session

1.4.3. Scales

The Fugl Meyer Scale (Lindmark adaptation) and the Motor Assessment Scale will be used to identify baseline characteristics in the sample group and the relationship with force torque (F/T) measurements will be investigated. Please refer to section 1.5.2.2 for the proposed scales

1.4.4. Natural Language Descriptions and audio recording

1.4.4.1. Operational definitions including delineation of tools and procedures

The following tools will be used to process the collection of the physiotherapist's patient descriptions (documents in digital text and audio form), to check processed documents, to extend the formal ontology, and finally to map taxonomy to ontology.

- **LinkFactory**®: formal ontology management system (OMS):
  In ALLADIN, LinkFactory® is used to extend the ontology LinkBase® for the neurorehabilitation domain and to map the taxonomy to the ontology.

- **LinkBase®**: medico-linguistic formal ontology:
  Used in ALLADIN as a source of (para)medical concepts; it will be extended for the domain of neurorehabilitation, in order to be used with TeSSI®/FastCode®.

- **Tessi®** : Terminology-Supported Semantic Indexing:
  In ALLADIN the system will be used to process the collected data; it will also be adapted to the new domain of neurorehabilitation via the ontology LinkBase®.

- **FastCode®**: semi-automatic ontology-based classification/coding middleware.
  In ALLADIN it will be adapted to the neurorehabilitation domain.

1.4.4.2. Audio recording

As can be seen in Figure 72 - Alladin Software Architecture, the physiotherapist will use a PDA to record patients' functional recovery. Software implemented by MULTITEL ASBL will allow for voice input to be indexed and for the addition of several extra pieces of information such as PT profile, estimation of the quality of the data recorded etc.

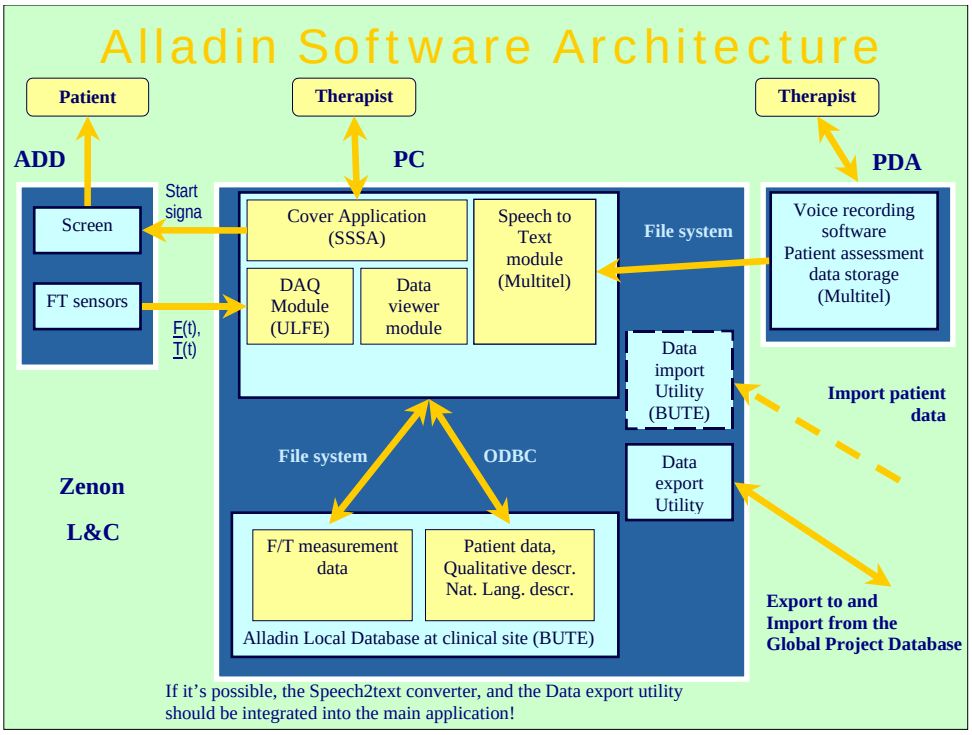


Figure 72 - Alladin Software Architecture

The PT will record the clinical phenomena as he/she prefers. Specific descriptions will be indexed into an XML document (Figure 73 - **Information**). The PT will be able to modify/update a set of parameters that will be further defined in close cooperation with the clinical partners.

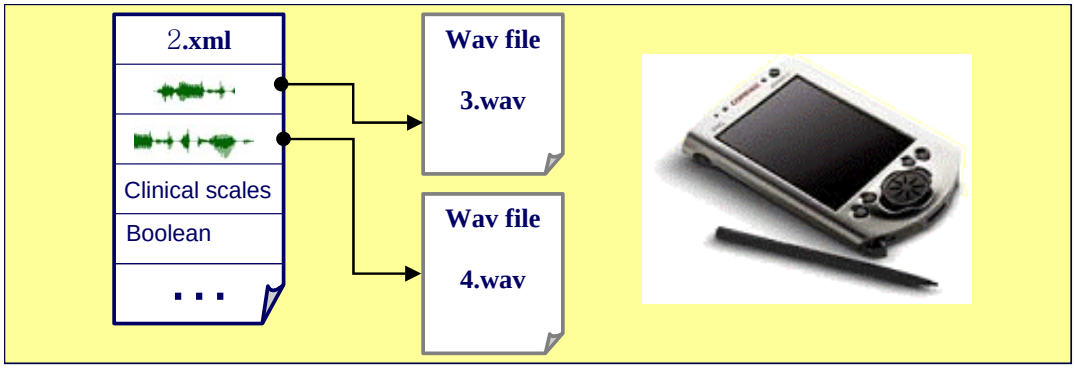


Figure 73 - Information storage on PDA

- Access time to SD is faster than standard PDA USB connectivity.
  [USB ⇔ 90kB / sec] whereas [SD ⇔ roughly 600kB / sec]
- Usability is the same as a floppy disc.
- Capacity: 256MB is standard. 512MB SD Cards are now available but are more expensive.

Now, according to the size of the databases needed for speech, some of the following information can be taken into account when considering database dimensions.

- 30' of speech = 55MB
- If we consider the previous point, there will be 100 patients with 34 assessments each giving a total of 3400 voice records. This means, if we allow 30' for each

assessment, we will have a maximum of 3400 * 30' of speech. That is to say ~ 184 GB.

1.5. Hypotheses, specific aims and final purpose

1.5.1. Reliability and validity

1.5.1.1.Reliability and validity of the ALLADIN diagnostic device

The ALLADIN Diagnostic Device (ADD) is designed for the measurement of isometric forces produced by stroke patients during rehabilitation. The scientific hypothesis is that the measured isometric forces correlate with the movements imagined and the movements completed during the ADL tasks that the patient is requested to do. At the end of the clinical trial we are likely to have 7000 or more force records which can prove the hypothesis through a statistical and data mining analysis. Today, when the ADD is designed, the question arises in another way: "are we studying what we think we are studying with the ADD?" and, are the measures we use consistent? *Reliability and validity theory* [121] informs us if it is worthwhile to use an isometric force measurement device for the detection of movement imagination and preparation. The definitions of these terms are as follows:

Reliability: the reproducibility of a measure. A measure is reliable if it yields similar results each time it is used on similar samples or, if its components yield similar results for the same or similar samples.

Validity: broadly defined, validity is the extent to which an observed situation reflects the true situation. *Internal validity* is a measure of the extent to which study results reflect the true relationship of an intervention to the outcome of interest in the study subjects. *External validity* is the extent to which the results of a study may be generalised beyond the subjects of the study to other settings, providers, procedures, diagnostics, etc.

The example below describes the relationship between reliability and validity in a practical way. Let's suppose that we want to measure the length and the width of a box, for example with a ruler, a tape, or a caliper. The dimensions of the box are known, for example it can be a precision gauge block. Imagine that for each measurement attempt you make a mark on squared paper with the co-ordinates you have measured: mark the length along the X axis and mark the width along the Y coordinate frame. After completing a series of measurements you will have one of the four pictures shown in Figure 74.

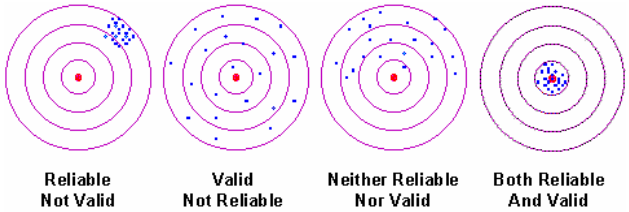


Figure 74 Relationship between reliability and validity

In the first picture, you have measured the dimensions consistently, but they are not the correct values indicated on the precision gauge block. That is, you are consistently

and systematically measuring the wrong value for the width and the length. This measure is reliable, but not valid (that is, it's consistent but wrong). The second shows dimensions that are randomly spread across the correct dimensions. You seldom measure the correct values but, on average, you are getting the right dimensions of the box (although not very well for individual measurements). In this case, you get a valid dimension estimate, but you are inconsistent. Here, you can clearly see that reliability is directly related to the variability, also called variance, of your measure. The third scenario shows a case where your co-ordinates are spread across the correct dimensions and you are consistently missing the correct dimensions. Your measure in this case is neither reliable nor valid. Finally, you consistently measure the dimensions of the box and your measure is both reliable and valid.

How can **validity** and **reliability** be estimated in concrete terms for the ALLADIN Diagnostic Device (ADD).

Estimation of the reliability of the ALLADIN Diagnostic Device

In the ALLADIN project three ALLADIN Diagnostic Devices will be used at three clinical sites for the measurement of isometric forces. The slightest variation in the measuring device, through the so called ALLADIN code we are generating, could mean the difference between CONTINUE or STOP rehabilitation treatment. The ALLADIN Diagnostic Devices then, must be reliable from one measurement to another. This type of reliability is called **Test-Retest Reliability** and is used to assess the consistency of a measure from one time to another. This is not sufficient however as, in the ALLADIN project, samples will be taken at three different sites. The three ADDs and all the spare parts must be manufactured is such a way that the three ADDs produce nearly identical measurements in the three geographical locations, independent of temperature, air pressure, humidity or other variables which might affect their readings. This type of reliability is called **Parallel-Forms Reliability** which is used to assess the consistency of the results of two tests constructed in the same way from the same content domain.

In order to estimate the reliability of the ADD potential errors that can occur during measurement should first be identified. According to the *True Score Ttheory* the observed value is equal to the true value and the error together across a set of measurements:

$X = T + e$

where X – observed value
T – true value
e – error

The simple equation of $X = T + e$ has a parallel equation at the level of the variance or variability of a measure. That is, across a set of scores, we assume that:

$var(X) = var(T) + var(e)$

where var – variance of the observed value

Reliability is formulated as the proportion of "truth" in the measure. It is defined as

R= var(T) / var(X)

We cannot calculate reliability because we do not know the true score. We can however estimate the true score component as the covariance between all observations of the same measure. With that in mind, we can estimate the reliability as the correlation between all observations of the same measure:

$$R = \frac{\sum_{i=1}^{n} \mathrm{cov}(X_i)}{\prod_{i=1}^{n} sd(X_i)}$$

where cov – covariance of the observed value
sd – the standard deviation of the observed value

It can be easily proven that reliability will always range between 0 and 1. The value of a reliability estimate tells us the proportion of variability in the measure attributable to the true score. A reliability of 0.5 means that about half of the variance of the observed score is attributable to truth and half is attributable to error. A reliability of 0.8 means the variability is about 80% true ability and 20% error.

Turning back to the ALLADIN Diagnostic Device, we can attempt to assess the reliability of the device indirectly, by assessing the errors it will have. When measurement errors are low, reliability of the measurements is high. An important design objective of the ADD is therefore to design it so that it is free of errors.

Three types of errors can be classified: random error, systematic error, and fatal error.

Let's start with the last. A fatal error can occur when the PT sets the ADD incorrectly, for example, the PT sets the ADD to the S size for an M size patient. Fatal errors usually can be identified immediately from the measurement results. Fatal errors cannot be corrected; hence the measurement has to be repeated when a fatal error is detected. Let's exclude any fatal error from this preliminary analysis.

Systematic errors are usually shared in the different measurements so they can be compensated for. Pilot tests will be conducted with the ADD to reveal possible systematic errors, but there are statistical procedures to adjust systematic errors when measurements are already made. A typical systematic error of the ADD could be the drift of the zero point of the force/torque sensors we use according to the temperature of the environment. A very easy way to exclude this systematic error would be the resetting of all force/torque sensors before each measurement. In so doing, environmental effects on the isometric force measurements can be ignored.

The third type of error, random error, is inherent in the ALLADIN Diagnostic Device. Random errors cannot be compensated for, and as seen in Figure 74, they are responsible for the reliability of the ADD. At the moment two sources of random errors are foreseen:

- positioning and mechanical errors,
- F/T sensor errors.

The *positioning errors* are related to the unrepeatable positioning of the patient in the ADD. Each patient will be measured 34 times during the ALLADIN clinical trial. Taking into consideration the budget constraints of the project, simple mechanical fixtures are used in the ADD to position the patient. The lower and the upper extremities will be positioned totally repeatable because both for the finger, the arm, and the foot devices three different settings will be available for an S, an M, and an L patient size (Figure 75). Setting of the devices into position will be by anti back-lash spring bolt mechanisms. The repeatability of the positions is considered to be ±0.1 mm. The rest of the patient's body however is not positioned by the device but by the physiotherapist. Centering the patient in the wheelchair will be made possible by polyurethane foam blocks. Positioning errors of the trunk due to improper sitting in the wheelchair can be in the range of ±30 mm. It cannot be predicted how these errors will affect the reliability of the isometric force measurements.

Mechanical errors associated with the ADD are, for example, deflection of the frame and backlashes of the mechanical interfaces to the changeable accessories. During isometric force measurement it is essential that force is measured without any such movement. To reduce mechanical errors the ADD will be designed as a rigid welded steel structure. The forces that have been considered for the selection of the F/T sensors will not cause noticeable mechanical strength and so, noticeable deformation of the frame. It is estimated that even at critical places the maximum deformation including the deformation of the transducer itself will be less than 0.01 mm. The most vulnerable parts of the ADD are the mechanical interfaces to the accessories. It is expected that each of them will be connected and disconnected at least 2000 times in each ADD. Some, even more, at least 6000 times in each ADD. We will design each of the interfaces as one-way-put, easy to lock, spring or weight pre-stressed, anti-backlash mechanisms. It is difficult to say anything about the errors caused by these interfaces. The ADD will be prototyped, tested, and modified through the conventional product development life-cycle.

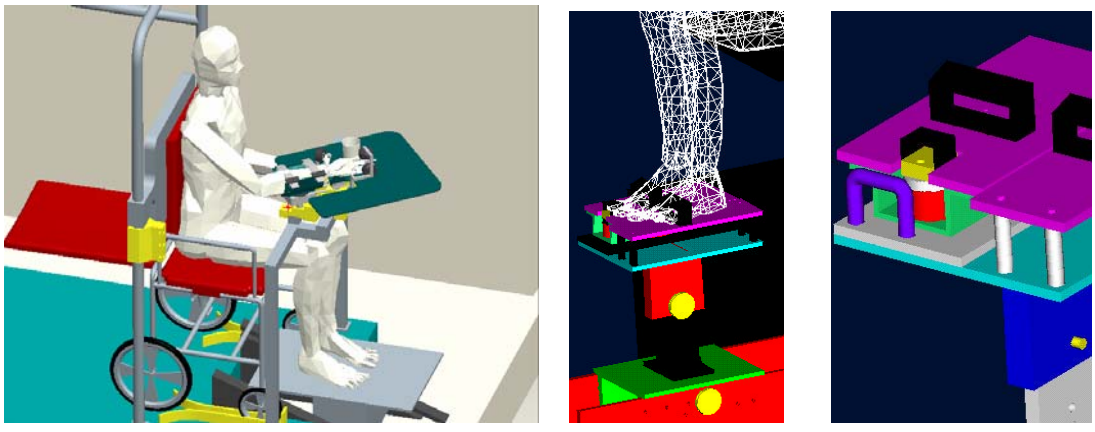


Figure 75 The conceptual design of the ADD (left), detailed design of the foot device (middle) showing the big toe and the foot fixations (right) on the right foot

The *sensor errors* are the only parameters we can assess at the moment. The manufacturer defines uncertainty for each 6 DOF FT sensor produced. The uncertainty

is a parameter that shows reasonably well the dissolution characteristic of a measurement value. In the calibration of the multi-component FT sensor, interference error as well as reproducibility error of the sensor, an error (relative expanded uncertainty) of the six-component force/moment sensor calibrator, an error due to the resolution of the indicator, an error due to the non-zero status without a load before and after calibration and a hysteresis error are generated. These influence the relative expanded uncertainty of the multi-component force/moment sensor. Therefore, the relative expanded uncertainty must include these errors. The relative expanded uncertainty shows the confidence limits of the multi-component force/moment sensor. National standards institutes generally use 95% as the confidence level. The error of the sensor therefore can be expressed as follows in N or in Nm:

$$e = \frac{U}{100}\frac{AL}{RL}$$

where U – is the relative uncertainty
AL – is the actual load of the sensor along the axis in N or Nm
RL – is the rated load the sensor along the axis in N or Nm

The sensors selected for the measurements have the following uncertainties[4]:

Type	RL [N]	RL [Nm]	F_x [%]	F_y [%]	F_z [%]	T_x [%]	T_y [%]	T_z [%]
Hand	145	5	1.50%	1.50%	1.25%	1.50%	1.75%	1.50%
Arm	130	10	1.25%	1.25%	1.00%	1.25%	1.25%	1.25%
Back, Foot	330	30	1.25%	1.25%	1.25%	1.25%	1.25%	1.25%

Reliability of the sensors can be significantly improved by introducing some special measures during the measurements. Resetting the sensor before each measurement can diminish the nominal load output error (typical value can be 1mV/V ± 20%), the zero setting error (typical value can be ± 0.2 mV/V), the sensitivity drift (typical value can be 0.5% / 10°C), and the zero drift (typical value can be 1% / 10 °C).

Experimental protocols will be designed and executed in Task 2.4 for the determination of the day-to-day and trial-to-trial reliability of positioning and FT measurements of the ADD. For example on three different days the same measurement cycle can be executed on the same ADD with a robot or alternatively with fixed weights and a laser interferometer simulating isometric force exertions.

Estimation of the validity of the ALLADIN Diagnostic Device

Construct validity seeks agreement between a theoretical concept and a specific measuring device or procedure [21]. Construct validity types can be further broken down into subcategories:

- Face validity
- Content validity
- Predictive validity
- Concurrent validity

[4] A 6 DOF FT sensor is usually accepted for industrial use if its uncertainty is below 3%

- Convergent validity
- Discriminant validity

In convergent validity, we examine the degree to which the operationalization is similar to (converges on) other operationalizations that it should theoretically be similar to. For instance, to show the convergent validity of a test of arithmetic skills, we might correlate the scores on our test with scores on other tests that purport to measure basic math ability, where high correlations show convergent validity. In the case of the ALLADIN Diagnostic Device we must show that movement imagination and movement preparation measured by isometric forces correlate with movement imagination and movement preparation measured by electromyography (EMG) [13-16] [20-22] [34] [69] [72] [108] [124]. There is scientific and experimental evidence that brain and muscle activities measured by EMG electrodes correlate with movement imagination and preparation even in the case of paretic patients.[35-37] [46] The ALLADIN project must prove that this is also possible with pure isometric force measurements.

To understand whether a piece of research has construct validity, three steps should be followed. First, the theoretical relationships must be specified. Second, the empirical relationships between the measures of the concepts must be examined. Third, the empirical evidence must be interpreted in terms of how it clarifies the construct validity of the particular measure being tested [121].

The challenge in detection of motion imagination by isometric forces is that motion imagination produces little muscle contraction, which in fact produces small muscle forces. Can force sensors detect these small changes? Are they sensitive enough? Do they have the required bandwidth? These questions arise first in connection with motion imagination. Motion preparation produces large forces which can be easily measured by multiaxis industrial force/torque sensors.

To study isometric force and torque measurements a preliminary measurement session was organised at NIMR. 6 healthy volunteers and 4 stroke patients participated in the study. The selected ADL exercise was reaching for a cup. The subject was asked to repeat the exercise 5 times. We have measured the isometric force/torque by the Uniforce F/T measuring system of A1 Ltd. Figure 76 shows the subject's arm fixed in the arm device.

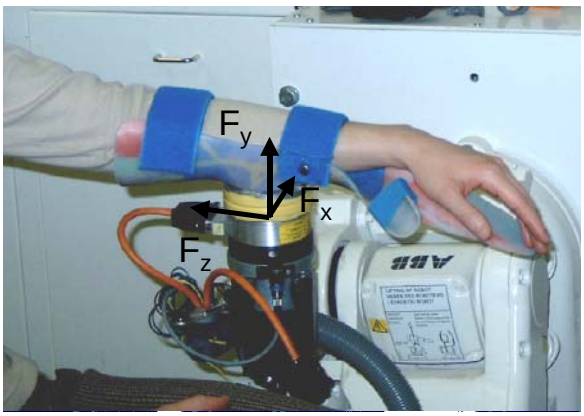


Figure 76 The arm device used during the preliminary measurements

The isometric force/torque measurements of patient #1 are shown in Figure 77. The patient was a 23 year old male with left sided spastic hemiparesis.

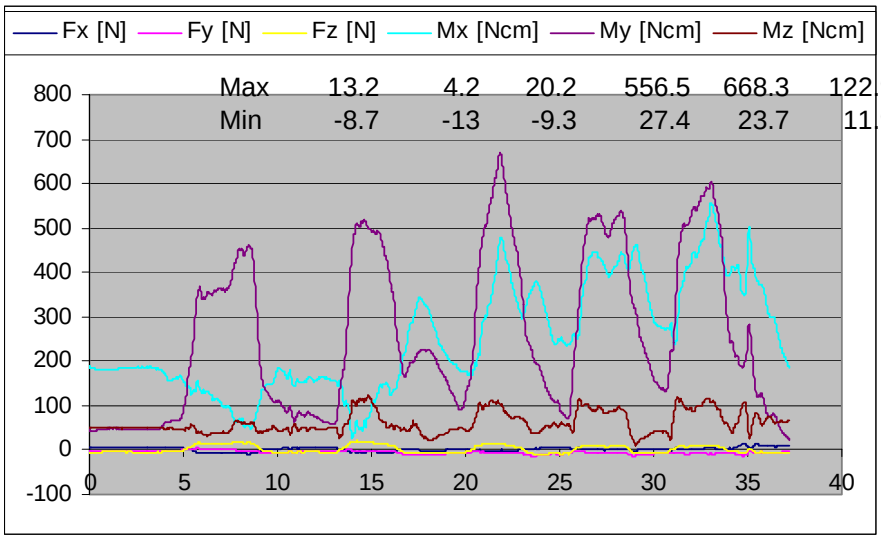


Figure 77 Isometric force/torque measurement of patient #1

The measured force and torque trajectories show clearly the development of isometric forces during the movement preparation phases. We are not sure however if it can show movement imagination. We are sure that the bandwidth and the resolution (Figure 78) of the industrial multiaxis force/torque measurement sensors are sufficient to show movement imagination, if any change in isometric forces is relevant to this motion control phase.

Please note that during the standard ALLADIN measurement protocol more time will be given to the patient for resting.

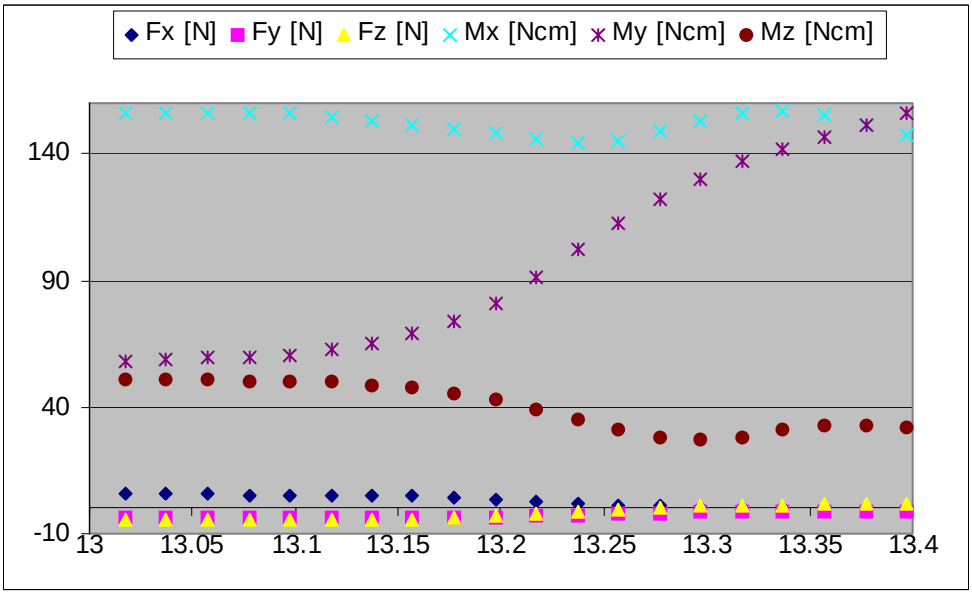


Figure 78 Isometric force/torque trajectories of patient #1 in the period of 13-13.4 sec

The theory of construct validity of the ADD, as well as experimental protocols, will be designed and executed in Task 2.4 also for the determination of the construct validity of the ADD.

1.5.1.2.The used scale(s)

1.5.1.2.1 Motor Capacity Assessment: the Fugl Meyer Scale (Lindmark adaptation)

The Lindmark adaptation of Fugl Meyer Scale was chosen because it combines the examination of functional limitations with underlying impairments. Objective scoring with a clear description for each point of the scale and well established levels of inter- and intra rater reliability make this a very suitable choice of outcome assessment for specific conditions.

The Motor Capacity Assessment was developed during the 1980's to provide a systematic evaluation of the motor capacity of individuals with cerebrovascular disease. It is based on the sensorimotor assessment of Fugl-Meyer et al, and modified by Lindmark. This assessment instrument tests the patient's motor control in terms both of differences between patients and, changes as a result of treatment. It is based on Brunstrom's stages of post stroke recovery [19].

The Lindmark adaptation of the Fugl Meyer Scale provides separate scored sections to test both impairment of upper and lower limbs and limitations of activities, specifically mobility and balance. The impairments examined include 1) ability to perform active movements, 2) skin sensation and 3) joint position sense of upper and lower limbs. The limitations of activity assessed are mobility and balance. Thus it assesses both active joint movements and task-related activities. The 4 point scoring system is clear. By assessing both affected and non-affected sides the instrument measures functioning as well as disability. This is important, as the patient will be dependent on the motor capacity of unaffected body parts. This scale gives a total description of the motor capacity of the stroke patient and not just of the hemiplegic side.

Additionally, individual or a number of sections can be used, depending on what information is required. This assessment instrument tests the patient's motor control in terms both of differences between patients and changes as a result of treatment.

Validity: The concurrent /convergent validity was calculated using Spearman's rank-difference correlation method to compare with the Fugl-Meyer Sensorimotor Assessment. [43] The Katz Index of ADL [68] and the Activity Index.[53] The correlation coefficients were between 0.85 and 0.98. The construct validity for Part A-Ability to perform active movements and, Part B-Ability to perform rapid movement changes, was estimated with factor analysis. Three factors emerged: upper extremity function, lower extremity function and standing leg movements and, co-ordination. Together these explained about 90% of the variance of the variables.

Reliability: The internal-consistency reliability of this assessment instrument was tested on 231 stroke patients. The different components of the motor score – ability to perform active movements and ability to perform rapid movements - gave coefficients

between 0.88 and 0.99. [27] The coefficient of mobility was 0.98 and that of balance was 0.90. This indicates that the items in this instrument are quite strongly related to each other and that the overall index of the repeatability or internal consistency of the scale as a whole is quite high.

Analysis level in the ICF framework: The Fugl Meyer Scale (Lindmark adaptation) can be described to represent a "domain" type instrument. It presents "a practical and meaningful set of related physiological functions, anatomical structures, actions, tasks…" Unlike most other instruments, it includes the concept of *functioning* of the unaffected body parts as well as that of *disability*. *Part A: Ability to perform active movements* combines an assessment of the impairment of upper and lower limbs with a certain amount of activity assessment. *Parts B: Ability to perform rapid movement changes, E Sensation, F: Joint pain. G: Joint motion,* are concerned solely with impairment. *Parts C: Mobility* and *D: Balance* at the analysis level of assessment of activity.

1.5.1.2.2 Motor Assessment Scale

The Modified Motor Assessment Scale is a stroke specific performance-based measure. It comprises 7 items

1	supine to side lying
2	supine to sitting over the side of the bed
3	balance sitting
4	sitting to standing
5	walking
6	upper arm function
7	hand movement - advanced hand activities

Table 16 The Motor Assessment Scale

Each item is scored from 0-7, with a higher score indicating optimal motor function.

Clear, guidelines are provided to optimise reliability.

Predictive validity has been established, arm function scores at 1 week and 1 month after stroke were good predictors of functional arm movement at discharge.

Convergent validity has been considered through comparison with scores on the FM and resultant significant relationships noted.

Inter-rater reliability - Mean kappa coefficients of 14 therapists	0.79-0.96.
Kappa coefficients for individual items	0.56-1.0.
Intra-rater reliability - Mean kappa coefficients	0.72-0.97.

Table 17 Reliability of the Motor Assessment Scale

1.5.1.3.Natural Language Descriptions

The input of physiotherapists is a prerequisite for developing a first-class ontology-based coding system with proper terminology that will cover the descriptions of the patient's status. The first role the physiotherapists will have is the composition of a corpus of documents containing the full spectrum of terms used in their practice. Secondly, they will indicate relevant terms and the meanings of these terms are couched in definitions given by the physiotherapists. Finally, the physiotherapists will

participate in the building of the classification system. Then, the knowledge engineer will be able to build an accurate representation of the domain by relying on the input of the physiotherapists.
The user's input will also be needed to map the milestones to the clinical expressions.

1.5.1.4.Audio assessments

"The reliability and validity of the audio assessment is one of the important key factors of the ALLADIN project. During the Dublin Recording Session (March 2004)[5], audio recordings were collected and analysed from a group of 20 persons with different voice characteristics. All recordings were analysed and checked in order to verify if the minimum requirements for the recognition engine was met. Speech recognition depends strongly on **the quality of the audio input**.

Main parameters are

The signal to noise ratio
The bandwidth of the microphone
The codec,
The true number of bits of the codec (depending on the total harmonic distortion)
if applied analog input filters.

Table 18 Main parameters for the quality of the audio input

The pilot study confirmed the reliability of the system used (IPAQ POCKET H1940)

Besides the audio quality, **the conditioning of the speech signal** is important. For this reason, immediate feedback about the recording conditions will be given to the user. This will guide him in a user friendly way to the optimal conditions for speech recognition. Optimal speech recognition, requires that the speech energy is somewhere between –32 dB and –6dB.

A first test with the recognition engine on more than 1000 terms has started and aims to prove the validity of the system

1.5.2. Characterization of clinical phenomena or existing conditions

1.5.2.1.The ALLADIN diagnostic device

The aim of the study is to identify if isometric force/torque measurements can measure and distinguish movement imagination and initiation during the six proposed functional tasks. At the same time the study will prove that for both features specific clusters in data will appear during recovery indicating a milestone or a marker. These markers will lay the foundations for a new method of steering neurorehabilitaton

[5] For a more detailed description see 5.3.2.4.1 and 5.3.2.4.2

1.5.2.2.The used scale

The aim of the study is to identify if there are significant links between the recovery that occurs post stroke as measured by the ADD and this recovery as measured by clinical scales and natural language descriptions.

1.5.2.3.Natural Language Descriptions

The precision, with which clinical phenomena will be characterized, depends on the comprehensiveness of the patient's descriptions and on the elaboration of the modeled domain. The more levels of granularity are modeled in the ontology, the more expressions will be covered. The medical ontology LinKBase® is the largest medical ontology, in the number of concepts it contains and in the number of relation types used for describing the domain. The knowledge engineers will enrich the medical ontology with new concepts and embed those concepts with relations to other concepts. If necessary, new relation types will be defined to allow field specific expressions.

1.5.3. Exploration of relationships

It is envisaged that clinical scales and natural language descriptions, which are typically used to assess the condition of a patient having physiotherapy, will, to some degree, correlate with isometric measurements. One significant difference between the isometric measurements, the clinical scales and the natural language descriptions is that the former are quantitative and latter qualitative (and are therefore open to a degree of interpretation by the individual Physiotherapist).

It is therefore expected that as a patients rehabilitation progresses there will be a marked difference in the isometric measurements gathered by the ADD in relation to the marks given on a clinical scale or the way the physiotherapist describes the patient.

An artificial example of this is shown below (Figure 79). This shows that as time progresses, and a patient's mobility improves, their ability to exert a force (or torque) increases. This is related to how a patients condition at the qualitative level will change from being wheelchair bound to being independent.

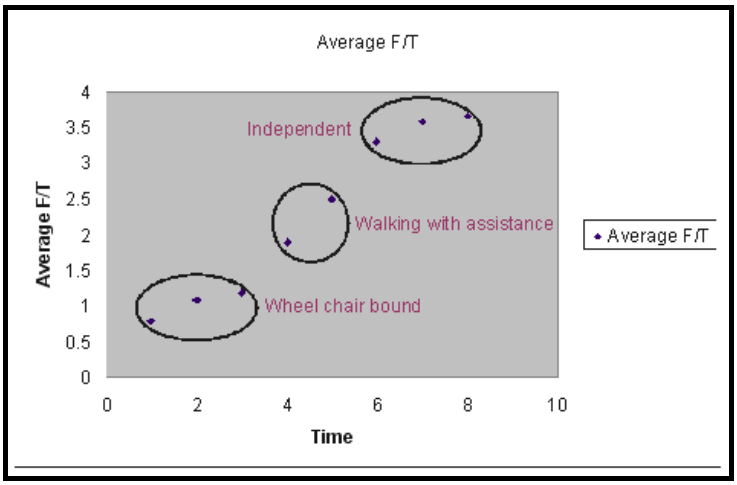


Figure 79 An artificial example of a relationship between F/T and functionality

When data mining is performed on the isometric measurements the results will be clustered into some analogue groups which will need to be identified with the assistance of a domain expert. This is because clustering and segmentation basically partition the isometric measurements so that each partition or group is similar according to some criteria or metric. These groups would then be identified by the domain expert. It is expected that these clusters will have a relationship with clinical scales and the way patient are described in natural language.

2. Sampling

2.1. Sample bias

2.1.1. Sample size calculation and Power

To calculate the proper sample size, we ensured that the statistical power will be reasonably high to detect reasonable departures from the null hypothesis. Otherwise, an experiment is hardly worth doing. The factors influencing power in a statistical test include:

1. What kind of statistical test is being performed. Some statistical tests are inherently more powerful than others.
2. Sample size. In general, the larger the sample size, the larger the power. However, increasing the sample size involves tangible costs, both in time, money, and effort. Consequently, it is important that sample size is “large enough,” but not wastefully large.
3. The size of experimental effects. If the null hypothesis is wrong by a substantial amount, the power will be higher than if it is wrong by a small amount.
4. The level of error in experimental measurements. Measurement error acts like “noise” that can bury the “signal” of real experimental effects. Consequently, anything that enhances the accuracy and consistency of measurement can increase statistical power.

Nevertheless, while we were gaining a better understanding of the magnitude of the problem, we realise that the nature of the work that is being done in ALLADIN is

different to that being done in a typical clinical trial because, in our case, the data is not being gathered to test a particular hypothesis, i.e. 'does rehabilitation technique A/B/C work?'. If the ADD was being used to test a hypothesis we could easily say x number of patient would sufficient to validate our hypothesis.

So, we focused on calculating the sample size required for our data mining experiment. Data mining is the process of sifting through and analyzing rich sets of domain specific data and then extracting information in the form of new relationships, patterns or clusters for decision making purposes. Conventionally, data is gathered to test an existing hypothesis (a top-down search, **Supervised Learning**). Alternatively, the existing data is mined and allowed to form natural clusters (a bottom-up finding, **Unsupervised Learning**).

In the Supervised Learning approach we use verification models which take a hypothesis and test its validity against the data. The emphasis is on the user who is responsible for formulating the hypothesis and examining the data to affirm or negate the hypothesis.

The number of learning examples needed for both training and pruning in the supervised learning approach can be estimated by the following formula:

$$size = \frac{K * \log_2(N)}{E}$$

Where: N is the number of attributes, K is the number of conditions needed to write down the smallest description of the target concept, and E is the percentage error that can be tolerated during the testing task. This formula indicates that we require more training examples as the complexity of the concept increases or the error decreases. However, in ALLADIN, as there are unknowns relating to this data, a size cannot be estimated, in particular N and K.

In the Unsupervised Learning approach discovery models differ in their emphasis in that the system is automatically discovering important information hidden in the data. The data is sifted to determine frequently occurring patterns, trends and generalisations without intervention or guidance from the user. Data mining tools can reveal a large number of facts about the data in as short a time as possible.

We agreed to follow the unsupervised approach taking into consideration that we wish to produce markers and milestones that will not be biased by PT's scales. Under this approach we can find several algorithms that provide high quality results.

Generally, for unsupervised techniques there is actually no minimum limit on the number of examples required for a clustering algorithm, as the given data will be grouped together based on their similarity. A domain expert typically performs the identification of the clusters – this is the case with ALLADIN as the markers/milestones are to be linked to the natural language descriptions by a PT.

By completing a literature survey and a search of available clinical databases we found some information concerning the number of the examples in data mining experiments

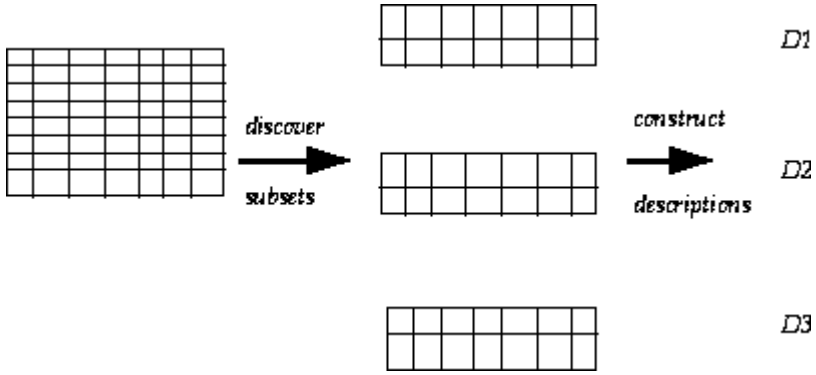
where measurements from clinical devices were used. The range was from 112 to 452, but in these experiments the number of the examples equals the number of patients.

In our data mining experiment we will use cluster analysis. Clustering is the process of creating a partition so that all the members (data-objects) of each set of the partition are similar according to some metric. A cluster is a set of objects grouped together because of their similarity or proximity. Objects are often decomposed into an exhaustive and/or mutually exclusive set of clusters. Clustering is referred to as a procedure of unsupervised learning, because it is not based on predefined classes, unlike the classification procedure (supervised learning) which requires the user to define one or more classes.

Different methods of clustering can be categorised according to:

- data types representing the objects
- ways of representing the clusters
- ways of organizing the clusters (hierarchical partitional, density-based, grid-based)
- algorithms that they use (Statistical, Conceptual, Kohonen Net, Fuzzy)

In an unsupervised learning environment the system has to discover its own classes and one way in which it does this is to cluster the **data-objects** in the database as shown in the following diagram. The first step is to discover subsets of related objects and then find **descriptions** e.g. D1, D2, D3 etc. which describe each of these subsets.



Clustering and segmentation basically partition the database so that each partition or group is similar according to some criteria or metric. Clustering according to similarity is a concept which appears in many disciplines. If a measure of similarity is available there are a number of techniques for forming clusters.
In our case, different clusters will represent different patients' states and from the clusters' descriptions we will try to discover markers and milestones. We will do this by finding attributes that present significant change between adjacent clusters.

In the ALLADIN project the data-objects we are going to cluster are not the patients but the "states" of the patients as each state is described by FT data on every visit.

Let $\mathbf{O_{i,j}}$ be our data-objects, where **i** is the patient (**i=1,2,…,I**) and (**j=1,2,…,J**) is the number of visit. So, the total number of our data-object will be: **I** x **J**.

If we suppose that we have 300 patients (I=300) and 30 visits per patient (J=30) then the total number of data-objects will be 9000. This sample size is sufficient according to the literature.

Each data-object may be represented as a vector with specific attributes (data): $\mathbf{O_{i,j}}(x_1,x_2,..,x_n)$. These attributes represent F/T data and probably some additional qualitative data.

We need to find markers and milestones from the produced descriptions of the clusters. In order to achieve this, the descriptions shall fulfill specific conditions. E.g. for some attributes monotony or other constraints may exist. The quality of the results, markers and milestones, depends not only on the sample size but also on data quality and algorithm selection.

To improve data quality we shall implement specific tasks for **pre-processing data**:

- **Data Cleansing** (Fill in missing values, smooth noisy data, identify or remove outliers, and resolve inconsistencies)
- **Data Transformation** (Normalization and aggregation)
- **Data Reduction** (Obtains reduced representation in volume but produces the same or similar analytical results)
- **Data Discretization** (Part of data reduction but with particular importance, especially for numerical data)

After pre-processing the data we may use several algorithms to produce the clusters. Some of these use statistical techniques (K_Mean, PAM, CRARA, CURE, DBSCAN, Wave-Cluster, etc), some use fuzzy techniques (Fuzzy C-Means) and some, other unsupervised Neural Networks (Kohonen Self-Organizing Maps).

In many commercial data mining and statistical analysis suites (SAS, SPSS, etc) and in software libraries, several pre-process and data mining algorithms have already been implemented.

We propose to select some of these algorithms depending on our data structure and to test the quality of the produced results before selecting the best combination. We hope to produce useful markes and milestones.

2.1.2.

2.1.3. Over and under representation

The sample selection shall comprise a representation for every different profile group of the patients' population. According to demographic data (age, sex, etc), the severity of patient's initial state and other historical data, groups of patients' profiles must be developed. The criteria for developing these groups shall be the impact level of the various values of these parameters to patient's recovery progress. For each group the percentage of its representation in the total sample must be calculated.

During the trial any possible over and under representation of the groups will be continuously assessed and deviations will be avoided where possible. Additionally, in the first interim report an assessment of over and under representations will be included and a strategy for the elimination of deviations will be proposed.

2.2. Accessible or experimental population

2.2.1. Consecutive sampling and length of study

In practice, it is sometimes difficult, if not impossible, to obtain a 100 % true random sample. The most common form of a non probability sample is a convenience sample or an accidental sample. With this method, subjects are chosen on the basis of availability. This is also the case in ALLADIN where the consecutive sampling method is used. This involves recruiting all patients who meet the inclusion and exclusion criteria as they become available.

2.2.2. Inclusion criteria in ALLADIN

Hemiparesis due to stroke
The brain impairment must be proved by CT or MRI
Minimum age is 18 years
The subject must be suitable to endure physical load during the measurements
The subject must be cooperative
Signed informed consent

Table 19 Inclusion criteria in ALLADIN

2.2.3. Exclusion criteria in ALLADIN

Restricted disposing capacity or legal incapacity
Prisoner
Movement or other disorder that makes it impossible for the patient to sit calmly during the treatment
Skin problem where use of an orthosis is contra- indicated
Patients shorter than 1530 mm
Patients taller than 1870 mm
Patients with a weight in excess of 110 kg

Table 20 Exclusion criteria in ALLADIN

2.3. Subject selection and recruitment by personal contact in clinical setting

Once the inclusion and exclusion criteria have been defined (see section 2.2), patient selection can begin.

Subjects will be recruited from the patient population in the researcher's facilities, which are:

1. The Maria Middelares Hospital (Gent Belgium)
2. St. James/Adelaide & Meath Hospital (SJH/AMNCH) (Dublin Ireland

3. Szent János Hospital (Budapest, Hungary).

2.3.1. The Maria Middelares Hospital (Gent, Belgium)

Unless stroke is very mild, the patient is admitted to hospital via the accident and emergency department. If his/her condition is critical he/she is admitted to the critical care unit, where he/she remains until stable.

Figure 80 Stroke Unit AZMMSJ Hospital

Afterwards the patient goes to the *stroke unit* or *geriatrics department* (Figure 80) where rehabilitation begins as soon as possible. Once the patient is discharged from hospital he/she remains in a suitable rehabilitation programme which is delivered either at home or in the rehabilitation ward (Figure 81) of the AZMMSJ hospital.

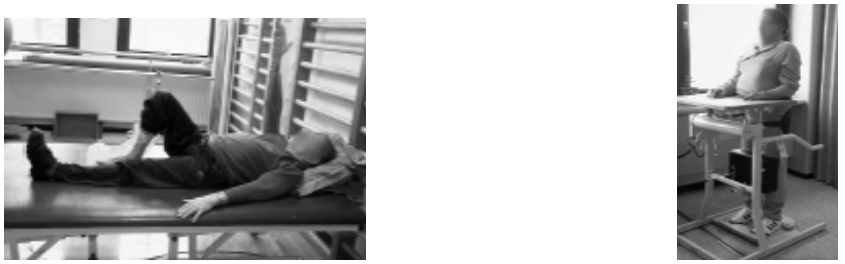


Figure 81 Rehabilitation department AZMMSJ Hospital.

When a new stroke patient is admitted the ALLADIN research team is immediately informed by the team of specialists who provide the relevant patient information and decide if the patient is suitable for participation in the study. The inclusion and exclusion criteria are re-checked and the patient's data is entered in the ALLADIN database.

This information is updated over the next few days with the results of medical investigations such as CT, MRI, EEG. This information is accessible from the Hospital Information System.

The team of specialists consists of:

Neurologists:	Dr. Algoed Luc Dr. Aers Isabelle
Rehabilitation specialists:	Dr Dhaese Marc Dr. De Grande Jan
Head nurse	Van de Kerkhoven Marc

If the patient is a possible candidate the ALLADIN team member in the hospital (Ms de Ruijter Sigried) explains the aim of the ALLADIN research and the possible risks and benefits. Having signed the consent form, a schedule for the testing is drawn up in agreement with the patient and the nursing and rehabilitation team. This schedule will be accessible in the hospital.

This team consists of:

Honoré Beatrijs
Neutjens Kristin
Janssens Jo
Vankerckhoven Ludo

At discharge further follow up is discussed and organised. In most cases a patient transportation service will be used to transport the patient to and from rehabilitation and testing sessions. This is done with the assistance of the head of the social department Ms Verplancke.

A special phone number will enable the patient to cancel or to change his/her appointment at any time.

2.3.2. SJH/AMNCH (Dublin, Ireland),

A patient with clinical symptoms of stroke is admitted to hospital through the *Accident & Emergency Department,* following referral by the General Practitioner. The patient undergoes physical examination, laboratory tests and a CT or MRI scan. Depending on their condition, they are admitted to the critical care unit, stroke unit, medical ward or medicine for the elderly unit.

The case is reported to the ALLADIN team based at the School of Physiotherapy (PT), Trinity College, St. James's Hospital. There is a close working relationship with the staff members of the physiotherapy department and the ALLADIN researchers will be present on site each day. This method of recruitment is routinely used for all of the research activities at the School of PT. A member of the research team visits and assesses the patient. Based on the ALLADIN inclusion /exclusion criteria the suitability of the patient is determined. If the patient is suitable testing can begin

immediately. If it is too early to make a decision, the patient is reviewed at a later stage.
If the patient is deemed suitable for inclusion and wishes to participate, the ALLADIN team member provides them with a Patient Information Leaflet and explains the aims and nature of the research and the possible benefits and risks. The procedure of the Joint Ethics Committee of SJH/ AMNCH will be strictly adhered to. When the consent form is completed a schedule for the testing is devised in agreement with the patient, the nursing staff and rehabilitation team. Global patient data is entered into the ALLADIN database and updated regularly.

The patient's length of stay in the acute hospital varies and, upon discharge, the patient may either return home or transfer to an appropriate aftercare facility such as a convalescent centre, or an extended care facility.

As the ALLADIN test centre will be located within the hospital, arrangements for follow-up testing will be made at the time of discharge. The transportation of patients to and from the test centre will be done under the guidelines of the health and safety regulations of the institution. Provision is made in the funding to provide transport to participants who will not use the hospital transport. This will be completed by driver trained in the appropriate handling skills. A contact phone number will be made available to the patient for rescheduling appointments.

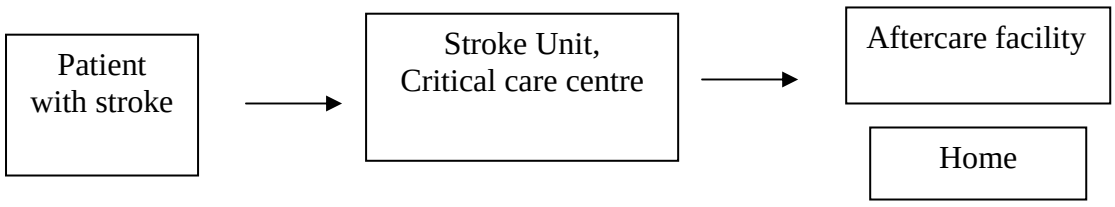


table 21 Members of the team at Trinity Centre for Health Sciences, Dublin

Principle Investigator	Emma K/ Stokes*
Research Fellow	AC Varghese*
	Bernadette Brady
PhD student	Caroline O'Connell*
Consultant Geriatrician	Desmond O'Neill

*Chartered Physiotherapists

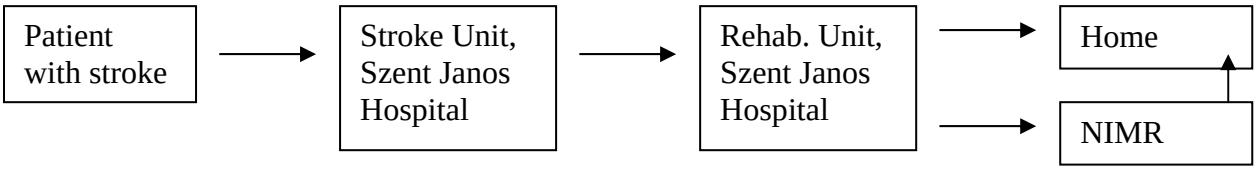
2.3.3. Szent János Hospital(Budapest, Hungary).

Patients with clinical symptoms of stroke are admitted to the Stroke Unit. They undergo physical examination, laboratory tests and CT scan. If the acute CT shows no haemorrhage or brain infarct, but the clinical symptoms of stroke are present, the case is considered and treated as ischemic stroke. A second CT is not done routinely, only if deemed necessary. Other investigations (carotis duplex scan, transcranial Doppler, EEG) are done in the days after admission if necessary.

On the first working day after admission the case is reported to the Rehabilitation UnitA doctor from the unit visits the patient and decides if he/she meets the inclusion

criteria. If it is too early to make a decision, the doctor re-visits the patient some days later. If the patient meets the inclusion criteria and signs the informed consent, the ALLADIN tests start immediately. The room for the ALLADIN research project will be located in the Rehabilitation Unit. While the patient is being treated in the Stroke Unit, he /she is transferred to the ALLADIN research room for the tests twice a week. At the end of the acute treatment, the patient is transferred to the Rehabilitation Unit. Treatment at the Rehabilitation Unit takes approximately three weeks. During this time the ALLADIN tests are done in this department.

Following discharge from hospital the patient may either go home and return to the rehabilitation unit for the tests or, if the patient requires further rehabilitation they are transferred to the National Institute for Medical Rehabilitation (NIMR). They return to Szent Janos Hospital for ALLADIN tests according to the research schedule. Following discharge from NIMR patient return home and continue to attend the Szent Janos Hospital for ALLADIN tests. Assistance with transport is provided if necessary.



The ADD will be located in the Rehabilitation Unit of Szent Janos Hospital. The patients come, or are transported, to the unit for the tests according to the schedule.

Figure 82 The Physiotherapy Unit at the Department of Rehabilitation of Szent Janos Hospital

Members of the team at Szent Janos Hospital:

Medical doctors entitled to include patients:	Gabor Fazekas Eszter Herczeg
Physiotherapists:	Monika Horvath Beata Kalnai Klara Martin
Occupational therapist:	Andrea Hering
Head nurse:	Maria Kiss

2.4. Guidelines for patient handling at AHS, TCD and NIMR

In the ALLADIN project patients will be transferred from bed to wheelchair and from one chair to another. If the patient is independent he/she can walk to the research room.

In all these cases 'patient handling' takes place. This is a specialized and important area in healthcare. Patient handling includes any task that involves moving or supporting a patient including carrying, pushing, pulling, lifting and lowering. Handling a person is more complex and unpredictable than handling an object. People may be heavy or hard to grip, and they must be treated with dignity, respect and consideration for their capabilities.

Before ALLADIN begins, the Ethics Committee at each participating centre will be consulted and informed of every possible risk. Such risk may be for example, measurement in the ADD. There may also be an element of risk associated with patient transport to and from the examination room and during set up of the measurement station.

Clinical trials are only carried out when there is assurance that subjects will be fully compensated for any damages which may result.

To minimise risk and increase safety a clear policy statement plan of patient handling has evolved. Safe handling implies safety not only for the patient but also for the investigator. Eliminating risks makes patient handling safer for caregivers. It also promotes patient independence and rehabilitation by making it easier for patients to help themselves.

The following items are carefully considered during the handling of patients in the ALLADIN project:

- Pain and response to pain
- Abnormal or restricted movements and abnormal reflex activity
- Hypersensitive areas or loss of sensation or awareness of body parts
- Impaired or "at-risk" skin which needs protection during handling
- Wet or slippery skin that needs extra care in some settings
- Incontinence, which may mean patients feel rushed and need extra time for the task
- Medical treatments or medications, which can affect capabilities in different ways at different times, so handling may need to vary
- Post-surgical handling, which may mean the wound must be protected, or movement restricted.
- Medical equipment, such as IV poles, which must be managed during the task
- Aggressive or abusive behavior, which may need 'calm and restraint' techniques

- The patient's ability to comprehend, co-operate and communicate, all of which influence the task.
- Any need for visual, hearing or mobility aids
- Whether glasses will help or hinder handling, for instance whether they will distort vision while walking
- Infectious or objectionable patients, who may require different handling
- Religious and cultural factors, which should be respected if it's safe to do so
- Personal preferences, which should be respected if practical and safe to do so
- A high risk of falls, in which case a falls risk assessment should be attached to the profile.

To attain the highest standards of patient and personnel safety the New Zealand LITE principles [6] will used in each participatings research center to determine the appropriate patient handling procedure. LITE is based on 4 principles: **l**oad, **i**ndividual, **t**ask and **e**nvironment. (Table 21)

	LITE Principles
Load	Load means patient characteristics that can affect the handling risk, such as age, gender, diagnosis, dependency, neurological status, size, weight, ability to co-operate, and fall risk
Individual	Individual means the capabilities of the investigators, such as language, education, training, physical limitation, stress and fatigue which can affect their ability to do the job safely
Task	Task means the nature of the task, what has to be done, how and when. Different tasks have different requirements, each needing assessment and a unique approach
Environment	Environment means the working environment, and covers factors such as facilities, staffing levels, culture and resources, all of which impact on how the task is done

Table 22 LITE principles

The following contributing factors are integrated in the methodology of the clinical trial

Load:

- time for the handling task is calculated
- patient profiles are part of the ALLADIN database and can be reviewed when needed
- minimum requirements (transferring patients from the chair to the measuring station needs a minimum of space) are set for the examination room and check procedures are available
- each task is explained and demonstrated to the patient and helpers are trained for the job
- clear instructions are prepared for each task
- hearing aids, needed glasses and mobility aids are checked before handling
- attention is paid to appropriate clothing and footwear

[6] New Zealand Department of Internal Affairs. 1992. Regulations – 25 April 2002 / B / Building Regulations 1992. Status Publishing

Individual:

- investigators are trained to identify risks and use equipment and techniques safely
- stress management is foreseen
- health and safety advice is prominently displayed at the different places in the hospital
- incentives to safely, not faster, are foreseen
- staff are encouraged to report health or other issues which could affect their ability to carry out handling operations safely
- attention is paid to suitable clothing and footwear

Task:

- sufficient space is calculated to perform the task and adapted equipment is used
- there will be regular breaks during the working day
- the need for squatting, kneeling or crouching is minimised
- all necessary tools are in place avoiding unnecessary movements
- equipment is stored in adapted closets to reduce retrieval time
- equipment is specially adapted to be used within the constraints of the facility
- maneuvers through doors, by beds and with wheelchairs are minimised.
- a specially adapted wheelchair is developed to transport patients from place to place. Transportation will be kept to a minimum
- staff are involved in the trial and selection of equipment

Environment:

- adequate space
- heating and lighting are adequate in the research room
- floors are non-slip and stable
- carpets are forbidden
- steps and slopes are well designed and properly lit
- attention is paid to potential “trip hazards” such as trailing wires, phone cables and lamp leads. Clutter will be removed immediately
- handling and access areas are kept tidy by special personnel
- handling is carefully planned for outpatients. A special patient transportation company is engaged.
- facilities are provided with securely positioned grab rails
- test equipment is adjustable, stable and suits the patient’s build and weight

This approach will be enforced and monitored throughout the trial. All unforeseen events will be recorded using a dedicated register. If necessary, patient handling guidelines will be adapted accordingly.

3. Experimental control

3.1. Confounding influence

3.1.1. Extrinsic factors

An extrinsic confounding factor is a variable that emerges from the environment and/or the experiment which is not directly related to the purpose of the study. Poor lighting or heating in the examination room are classic examples. Also, new approaches in stroke treatment such as the use of amphetamines, neuroprotective or thrombolytic therapies can influence the normal course of recovery substantially and are therefore considered as extraneous confounding influences.

3.1.2. Intrinsic factors

The most important intrinsic factors are - the sudden occurrence of depression with lack of motivation, short term psychological reactions such as paroxysmal anxiety, subacute confusional states, embarrassment or fear.

3.1.3. Testing effects

The ALLADIN device is a measuring device but it includes tasks that can have a therapeutic value. Consequently, it is possible that the outcome of the study population will be influenced positively in comparison with the general population.

3.1.4. Reactive measurements

After repetitive testing the patient can learn how to influence a particular measurement. To seek attention he can for example, fake bad performance. Inspection of the F/T measurements by a skilled therapist can help to detect some of these confounding influences and overcome the problem.
Also the fact that the patient receives all attention during the measurements can temporarily improve his skills. This will only be a transient factor however as the patient becomes accustomed to the situation during consecutive measurement sessions.

3.1.5. Instrumentation effects

The following confounding testing effects are anticipated:

Starting/stopping an exercise –calibration
Deviation of sensor position/location on patient
Therapist consistency in setting up the equipment
How different therapists explain to patients how to carry out the exercises
Multi-centred trials (different population characteristics)

3.2. Blinding

Blinding (sometimes called masking) is used in research to eliminate bias from a study as human behaviour and expectations may influence findings. There are different degrees of blinding. For example, in single-blind trials the patients do not know what trial treatment they have been assigned to, but their doctors know. A danger of using single-blind trials is that the doctor might be biased in the decisions he/she makes about the patient's condition or, apparent side effects of the treatment or, any other therapy the patient receives. To avoid this, double-blind trials can be conducted where neither patients nor doctors know which treatment an individual patient has been assigned.

The aim of the ALLADIN trials is not to investigate the effect of a new treatment or physiotherapy but to detect markers and milestones of recovery by analysing data obtained from patients performing ADL tasks. Two issues will be of importance to avoid biased results.

Firstly, the team that evaluates the data to determine hidden patterns should ideally have no knowledge of the physiotherapist's assessment of the patient. This will be the initial approach and the only label attached to the data will be the patient number and the visit number. If milestones or patterns are believed to have been found, they will be mapped to the actual patient's state and progress by the clinical partners in order to verify if correlations actually exist or, if the milestones were a product of the data manipulation. It may happen that during data analysis additional information about the patient is required. If this is the case, the team analysing the data must provide clear justification to the clinical partners as to why the additional information is needed. Thorough discussions between the analysing team and the clinical partners will minimise the risk of a biased evaluation.

Secondly, even if the trial does not provide a new treatment a patient may wrongly get the impression that the trial has a secret meaning or, that he/she will be evaluated based on the results. He/she may then subconsciously try to maximise performance during the ADL tasks and therefore the data obtained will not correspond to the patient's actual state. To avoid this, it must be clearly explained to patients that participation in the ALLADIN project will have no short-term influence on their life but that the research aims to provide predictive diagnostic information at its conclusion. The patients must understand that the measurements being made have no value to individual patients but only in the overall context of the trial.

4. Experimental design

4.1. Measurement of variables

Three sets of variables will be measured, including baseline demographic and clinical data, on each participant in the ALLADIN clinical trial. The variables will be

Force/torque (F/T) measurements made by the ALLADIN diagnostic device.
Clinical scales which will be standardised outcome measures (SOM)
Clinical descriptions (CD)

4.2. Individual measurement sessions

One direct subject hour comprises 30 minutes of F/T measurements and 30 minutes of clinical scales and/or descriptions. Each subject has a minimum of 1 and ideally 2 direct subject hours for the first 8 weeks and 1 per week thereafter for 18 weeks. The number of direct subject hours available will dictate the number of active subjects in the study. Local working hours, local existing patient schedules, portering, transport etc, influence the total number of direct measurement hours available in each day in each of the three centres.

4.3. Direct subject hours and the total number of participants

As outlined in the description of work, there will be 64 weeks in total to gather data. 40 weeks are required to recruit participants and also to enable a 6-month follow-up for the last subjects recruited. Each subject has data gathered for 6 months or 24 sessions. Based on an estimate of 50 direct subject hours per week and an estimated 3 new subjects per week, this will enable the inclusion of approximately 70 subjects per centre. This does not take into account participants who drop out of the study and for whom complete datasets will not be available.

4.4. Measurement cycles, number of measurements

There will be two measurement cycles of one-hour duration – session A and session B. Each represents one direct subject hour. Session A will comprise 30 minutes of force torque measurement and 30 minutes of clinical descriptions. Session B will comprise 30 minutes of force torque measurements and 30 minutes using standardised outcome measures (SOM) – the MAS and the FM, each taking 30 minutes to complete. They will be repeated during alternate sessions. This will yield a total of 34 F/T measurement cycles, 15 clinical descriptions (each of 30 minutes duration) and 16 SOM's- 8 MAS and 8 FM.

Session	Force torque measurements	SOM	SOM	CD	CD
0					
1.1	Force torque 1			Clinical description 1	
1.2		Fugl-Meyer 1			
2.1	Force torque 2			Clinical description 2	
2.2		Motor assessment scale 1			
3.1	Force torque 3			Clinical description 3	
3.2		Fugl-Meyer 2			
4.1	Force torque 4			Clinical description 4	
4.2		Motor assessment scale 2			
5.1	Force torque 5			Clinical description 5	
5.2		Fugl-Meyer 3			
6.1	Force torque 6			Clinical description 6	
6.2		Motor assessment scale 3			
7.1	Force-torque 7			Clinical description 7	
7.2		Fugl-Meyer 4			
8.1	Force torque 8			Clinical description 8	
8.2		Motor assessment scale 4			
9	Force torque 9			Clinical description 9	
10		Fugl-Meyer 5			

11	Force-torque 10		Clinical description 9
12		Motor assessment scale 5	
13	Force torque 11		Clinical description 10
14		Fugl-Meyer 6	
15	Force torque 12		Clinical description 11
16		Motor assessment scale 6	
17	Force torque 13		Clinical description 12
18		Fugl-Meyer 7	
19	Force torque 14		Clinical description 13
20		Motor assessment scale 7	
21	Force torque 15		Clinical description14
22		Fugl-Meyer 8	
23	Force torque 16		Clinical description 15
24		Motor assessment scale 8	

Table 23 Outlines the proposed mechanism by which the measurement cycles will take place for one individual participant

5. Data Management

5.1. Data acquisition

Two parallel processes are completed simultaneously during the clinical investigation. Patient measurement data is produced at the clinical sites, while at the same time, previously recorded measurements are analyzed by the information processing partners. It is necessary to develop a system, which stores the collected data, controls the data flow between the geographically distributed locations, and provides systematic backup of the entire database.

The following data will be collected:

- Patient data and case history
- Standard Outcome Measure (SOM)
- Natural language description of the patient's status
- Voice records of the descriptions
- Force/torque measurement records of the ADL exercises

5.2. Data coding

Acquisition and storage of more than 200 patient's data needs an efficient transfer of data between the data collection points and the central database, and also between the central database and the analysis points. The Internet was an obvious choice as a means of transferring the data between data acquisition and data using points. In this chapter we seek to determine if data coding is necessary for the transfer of ALLADIN data through the Internet.

The data recorded during the clinical trial is the patient's personal data, so the rules stipulated by the EN ISO 540 standard, by the 95/46/EEC decree, and by the 93/42/EEC decree will be followed.[26] Personal data used outside clinical partners' Electronic Patient Record systems will be coded so that patient's identification cannot be determined during electronic transfer. After inclusion in the trial, every participant receives an ID: between AHS-001 and AHS-150 in Gent, between TCD-001 and TCD-150 in Dublin, between NIMR-001 and NIMR-150 in Budapest. Only documentation related to the trial contains these IDs. A list, including the patient's name, ID, address, date of birth, and national insurance number is also compiled. This list is stored separately from the Case Report Forms (CRFs), in the office of the trial

leader, together with the signed informed consents. The list containing the patients' personal data must only be used at the medical centre participating in the trial. Use of such data outside the participating centre is strictly forbidden.

The above methodology removes any "personality" from the collected historical, biomedical, and clinical data, so it can be safely transferred through the Internet without the need for further electronic encryption such as, for example, that used in electronic signatures or for e-banking. Of course the data will be coded before, and decoded after, transfer through the Internet in order to maintain the integrity of the data. Checksum, binary coding, or similar techniques will be used for this purpose. All patient data available through the Internet will only be available for the project partners through secure Web access.

The patient will be informed about the handling of his/her personal data before inclusion in the clinical trial. The signed informed consent allows us to handle the patient's data in the manner described above.

5.3. Data entry (preliminary data)

1. Clinical description

    1.1 Select patient profile
    1.2 Define new patient profile
    1.3 Exit

2. Measurements & Data
    2.1 Set-up menu
        2.1.1 Sequence order
        2.1.2 Sequence duration
        2.1.3 Sensors calibration

    2.2 F/T measurement session
        2.2.1 Show ADLi (i=1..6)
        2.2.2 Data acquisition
            2.2.2.1 Start
            2.2.2.2 Stop
        2.2.3 Data visualization

    2.3 Speech2text data
        2.3.1 Import data from Speech2text module
        2.3.2 Data visualisation
        2.3.3 Delete data
        2.3.4 Save data on Local Database

    2.4 Operations on Local Database (DB)
        2.4.1 Save F/T data measurement on DB
        2.4.2 Load F/T data measurement (view previous data) from DB
        2.4.3 Delete F/T data measurement
        2.4.4 Repeat F/T data measurement
        2.4.5 Save voice2text data on DB
        2.4.6 Load voice2text data on DB
        2.4.7 Delete voice2text data on DB

2.5 Exit

5.3.1. Human machine interface for the patient

5.3.1.1.Instructions, video for patients

Preliminary data can be found in section 1.4.2.5.3

5.3.2. Human machine interface for the operator

5.3.2.1.Isometric measurements

Preliminary data can be found in section 1.4.2.5.3

5.3.2.2.Audio recording

5.3.2.2.1. Pilot recordings free descriptions

Audio recordings play an important role in ALLADIN in the sense that all natural language descriptions are recorded by a PT and are stored. The first Audio Recording Sessions took place in Dublin. The sessions were organized to record 40 different pages of descriptions, including specific terminology. Descriptions were read by 20 native speakers (male and female).

The main goals of the Audio Recording Sessions are:

- Extracting specific PT keywords from descriptions that are relevant to the terminology of physiotherapy.
- Linking these keywords through a specific PT ontology
- Achieving the speech recognition grammar and building the ontology.

The recording conditions have to be taken into account.
A strategy has been elaborated in order to achieve this. Each person recorded 4 pages of description during a session which took 45 minutes. Each description was read by 20 different native voices.

An example of a description which was read by a native speaker is as follows -

Description 1

This patient was referred for physiotherapy following admission with a stroke. He presents with a hemiplegia on the left side but does not have a hemianopia and test of inattention tests were also negative. Left-sided hemiplegic limb pain was reported, most especially left hip pain and hand pain. The nursing staff reported that he was able to rise from sitting to standing with no help. The patient was in bed, poorly positioned in half crook lying, when I entered the room. He claps his hands with the offer of rehabilitation. I suggested that we would go to the physiotherapy gym, so that I could have more space to perform gait analysis. I ask him how he is getting on with general functional mobility and transfers and he reports that getting from a

chair to bed and getting up stairs was proving difficult. He also complains that his arm feels abnormally heavy when it is lifted above his head, highly similar to the sensation of a dead arm and this is resulting in problems when he tries to dress and shave. Before getting out of bed, a heel-to-shin test was completed to ensure co-ordination was intact. It was impossible to perform the flexor synergy in supine position. On getting from the bed to the standing position he pushes on his arms using elbow extension to propel his body forward. He will compensate with the unaffected side. The patient showed signs of tendency to ignore the left side of space. He assumes the standing position with the head and neck leading the direction of movement. Head, neck and trunk flexibility all appeared normal. Once in the standing position there is evidence of hyperactive hamstring co-contraction. He uses an inadequate base of support. A full gait analysis was then carried out. Gross movements seemed to be quiet normal. When gentle resistance to movement was applied he showed signs of holding rigidly his position. Full extension of the hip and knee joints was present, showing adequate activation of the iliopsoas muscle group. Left hip lateral rotation and medial rotation were half normal range of movement. Hip, knee and ankle flexion ranges were all within normal limits. However, inadequate limb clearance on the left was leading to hip hiking on the same side. He was placing his heel forward in a position of a short step. Incomplete knee extension during the late swing and early stance phase was occurring. The patient was incapable of hip abduction and so hip abduction beyond range was obtained from this elevation of the pelvis.

5.3.2.4.2. Pilot recordings of expression used in physiotherapy

As three PDAs and three SD cards were purchased for the Dublin recording session (by Multitel, AHS and TCD), three recording sessions took place in parallel as shown in the schedule below.

Time						
10.00-10.45	V1	D1,D2,D3,D4	V8	D14,D15,D16,D17	V15	D27,D28,D29,D30
10.45-11.30	V2	D1,D2,D3,D13	V9	D14,D15,D16,D26	V16	D29,D30,D31,D32
11.30-12.15	V3	D27,D4,D5,D6	V10	D28,D17,D18,D19	V17	D31,D32,D33,D34
12.15-13.00	V4	D5,D6,D7,D8	V11	D18,D19,D20,D21	V18	D33,D34,D35,D36
14.00-14.45	V5	D7,D8,D9,D10	V12	D20,D21,D22,D23	V19	D35,D36,D37,D38
14.45-15.30	V6	D9,D10,D11,D12	V13	D22,D23,D24,D25	V20	D37, D38, D39,D40
15.30-16.45	V7	D11,D12,D13,D40	V14	D24,D25, D26, D39		

Table 24 Organization of the Dublin recording sessions

Each session was completed in a different room (three rooms had been booked). Some audio recordings -PDA1 (AHS)- were done in a small room (Fig. 83), to reflect the environment where PT would treat patients.

Figure 83 - Small room

Other recordings - PDA2 (TCD)- were done in a medium size room (Fig. 84), to reflect a hospital room. Some noises were produced during the recordings such as grasping a chair, moving a bed etc.

Figure 84 - Medium room

The third group of recordings -PDA3 (Multitel)-were done in a corridor (Fig. 85). This reflects the situation where a PT records his diagnosis in a place where a patient waits for some specific assessment (radiology or scanner).

Figure 85 - Corridor

Each person read four A4 pages of description. Each description was read twice, by different persons, and stored on an SD Card (256MB).

During one audio recording slot, we asked the readers:

- Not to read the description but to pronounce the text as if they were talking instead of 'reading'. Indeed, reading is more or less a passive task whereas talking is more situation driven.
- To hold the PDA approximately 20 cm (which is the ideal position) from their mouth: and, to keep the PDA in a natural position.
- To speak normally.

During a 45 minutes slot, 5 minutes were dedicated to explaining what was required. 15 to 20 minutes were taken to record the 4 pages. This allowed enough time to organize the recordings and to rephrase if something had been misread. It also helped to minimise stress. In the final 15 to 20 minutes, we copied the SD card contents onto a PC and checked that the minimum audio requirements had been reached (the signal has to be between –32db and –6db, the DC offset has to be less than 1%, …). Some other prerequisites –related to microphone quality- would not have altered the end results. Moreover, we checked to ensure that the user did not speak too loudly.

At the conclusion of the recording sessions we established the following :

- Almost 452 MB of speech was collected in Dublin.
- Battery status of one PDA after 1 day of work was 39%.
- PDA1 (AHS): 124.044.762 Bytes
- PDA2 (TCD): 169.260.645 Bytes (this PDA contained more information because it was used with microphone in different positions.
- PDA3 (Multitel) : 125.043.773 Bytes

In the near future, the perplexity of grammar used in physiotherapy will be further estimated. Therefore the implementation of a piece of software for

testing the spotting with the recognition engine is planned. MULTITEL's role will be as follows:

1) To segment the speech files into sentences (manually).

2) To build a grammar with the underlined keywords to be recognised by the recognition engine,

3) To implement the software which must permit the following:
   a. load a wav file from the software.
   b. launch a recognition process that will attempt to extract keywords from the PT descriptions recorded in Dublin.
   c. produce a text as output in order to compare results.
   d. improve the granularity/perplexity of the grammar and so on in order to estimate the sensitivity of the recognition engine regarding the recordings performed in Dublin.

4) The prototype will produce the following peace of information:

   a. If a description corresponds with:

      "*This patient was referred for physiotherapy following admission with a stroke. He presents with a hemiplegia on the left side but does not have a hemianopia and test of inattention tests were also negative.*

   b. And a PT says: (this example is only to show the purpose and contains mistakes regarding the meaning).

      "*I don't know why but yesterday I encountered a hemiplegia on the left side of the road and had a hemianopia with inattention tests and they were also negative.* "

   c. Depending on the way we will build the grammar, the recognition engine may not be able to produce the expected result.

   d. A grammar can be built as follows:

```
#!FSG

<BOS>=alt(
        *[GARBAGE]
 )alt;

<WORDS_TO_BE_SPOTTED>=alt(
hemiplegia
hemianopia_and_test_of_inattention_tests
*[GARBAGE]
)alt;

<EOS>=alt(
        *[ GARBAGE]
 )alt;

<START>=seq( opt( <BOS> )opt
```

```
                    alt( <WORDS_TO_BE_SPOTTED> )alt
                    opt( <EOS> )opt
    )seq;
```

e. The resulting output, if the audio recording is good, will then be, in the software:

> "[…] hemiplegia […]"

Now, as you see, if the grammar is not well written, we can miss something here because the PT did not say the expected **item** as written in the grammar. I mean:

> *hemianopia with inattention tests* (said by the PT)
> is different than *hemianopia_and_test_of_inattention_tests* (expected in the grammar)

So, we could have built it like that:

old:

```
<WORDS_TO_BE_SPOTTED>=alt(
 hemiplegia
 hemianopia_and_test_of_inattention_tests
*[GARBAGE]
)alt;
```

new:

```
<WORDS_TO_BE_SPOTTED>=alt(
 hemiplegia
        opt( <SPECIFIC_SEQUENCE_WITH_GARBAGES> )opt;
        *[GARBAGE]
 )alt;

< SPECIFIC_SEQUENCE_WITH_GARBAGES>=alt(
        seq( hemianopia *[GARBAGE] test of inattention_tests )seq;
        seq( hemianopia *[GARBAGE] inattention_tests )seq;
 )alt;
```

Then, the resulting output, if the audio recording is good, will be, in the software, something like:

When PT says:

> "*I don't know why but yesterday I encountered a hemiplegia on the left side of the road and had a hemianopia with inattention tests and they were also negative.* "

The software may give as a result:

> "[…] hemiplegia […] hemianopia […] inattention_tests […]"

Afterwards, we may possibly be able to correct misunderstandings from the recognition using confidence levels and colours something like the possibility of clicking on a word to hear the corresponding speech.

"[…] hemiplegia […] hemianopia […] inattention_tests […]"

When the user clicks on inattention_tests, he can hear something like in the attention tests and the user interface will propose him all variants that are close to it containing, in fact, the nBEST values from the recognition engine linked to this word.

Green colors can be words with confidence levels over a certain value and red colors can be words below another value to be set in an adjustment panel like in

Figure 86 – Confidence level settings.

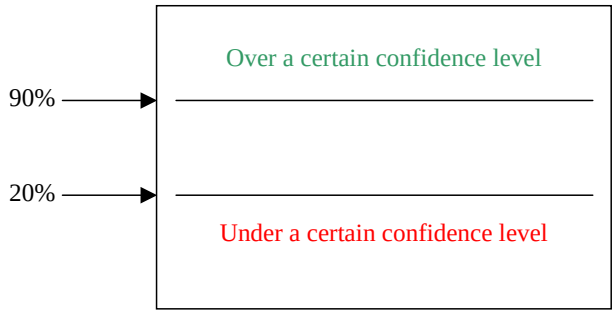


Figure 86 – Confidence level settings

5.4. Data processing

Unsupervised Learning Classification

Data mining is the process of sifting through and analyzing rich sets of domain specific data and then extracting information in the form of new relationships, patterns or clusters for decision making purposes.

Conventionally, data is gathered to test an existing hypothesis (a top-down search, Supervised Learning). Alternatively, the existing data is mined and allowed to form natural clusters (a bottom-up finding, Unsupervised Learning).

In the Supervised Learning approach we use verification models which take a hypothesis from the user and tests its validity against the data. The emphasis is on the user who is responsible for formulating the hypothesis and analysing the data to affirm or negate the hypothesis.

In the Unsupervised Learning approach we use discovery models where the system automatically identifies important information hidden in the data. The data is sifted in search of frequently occurring patterns, trends and generalisations without intervention or guidance from the user. The discovery or data mining tools aim to reveal a large number of facts about the data in as short a time as possible.

In ALLADIN we decided to follow the Unsupervised Learning approach taking into consideration that we wish to produce markers and milestones that will not be biased by PT's scales. Using this approach we can find several algorithms that provide high quality results.

Unsupervised classification refers to situations where the objective is to construct decision boundaries based on unlabeled training data. Unsupervised classification is also known as data clustering which is a generic label for a variety of procedures designed to find natural groupings, or clusters, in multidimensional data, based on measured or perceived similarities among the patterns. Category labels and other information about the source of the data influence the interpretation of the clustering, not the formation of the clusters.

Unsupervised classification or clustering is a very difficult problem because data can reveal clusters with different shapes and sizes (Figure 87). A number of functional definitions of a cluster have been proposed which include: 1) patterns within a cluster are more similar to each other than are patterns belonging to different clusters and 2) a cluster consists of a relatively high density of points separated from other clusters by a relatively low density of points. Even with these functional definitions of a cluster, it is not easy to come up with an operational definition of clusters. One of the challenges is to select an appropriate measure of similarity to define clusters which, in general, is both data (cluster shape) and context dependent.

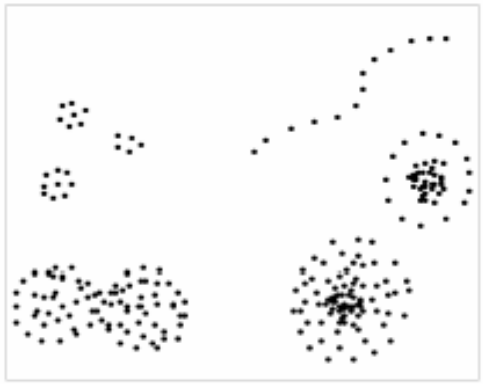


figure 87 Clusters with different shapes and sizes

Cluster analysis is a very important and useful technique. The speed, reliability, and consistency with which a clustering algorithm can organize large amounts of data constitute overwhelming reasons to use it in applications such as data mining, information retrieval, image segmentation, signal compression and coding, and machine learning. As a consequence, hundreds of clustering algorithms have been proposed in the literature and new clustering algorithms continue to appear. However, most of these algorithms are based on the following two popular clustering techniques: iterative square-error partitional clustering and agglomerative hierarchical clustering. Hierarchical techniques organize data in a nested sequence of groups which can be displayed in the form of a dendrogram or a tree. Square-error partitional algorithms attempt to obtain that partition which minimizes the within-cluster scatter or maximizes the between-cluster scatter. To guarantee that an optimum solution has been obtained, one has to examine all possible partitions of the n d-dimensional patterns into K clusters (for a given K), which is not computationally feasible. So, various heuristics are used to reduce the search, but then there is no guarantee of optimality.

Partitional clustering techniques are used more frequently than hierarchical techniques in pattern recognition applications. Recent studies in cluster analysis suggest that a user of a clustering algorithm should keep the following issues in mind: 1) every clustering algorithm will find clusters in a given dataset whether they exist or not; the data should, therefore, be subjected to tests for clustering tendency before applying a clustering algorithm, followed by a validation of the clusters generated by the algorithm; 2) there is no “best” clustering algorithm. Therefore, a user is advised to try several clustering algorithms on a given dataset. Further, issues of data collection, data representation, normalization, and cluster validity are as important as the choice of clustering strategy.

The problem of partitional clustering can be formally stated as follows: Given n patterns in a d-dimensional metric space, determine a partition of the patterns into K clusters, such that the patterns in a cluster are more similar to each other than to patterns in different clusters. The value of K may or may not be specified. A clustering criterion, either global or local, must be adopted. A global criterion, such as square-error, represents each cluster by a prototype and assigns the patterns to clusters according to the most similar prototypes. A local criterion forms clusters by utilizing local structure in the data. For example, clusters can be formed by identifying high-density regions in the pattern space or by assigning a pattern and its k nearest neighbors to the same cluster.

The technique of conceptual clustering or learning from examples can be used with patterns represented by nonnumeric or symbolic descriptors. The objective here is to group patterns into conceptually simple classes. Concepts are defined in terms of attributes and patterns are arranged into a hierarchy of classes described by concepts.

Overall description of data processing in ALLADIN

In ALLADIN three different set of data will be collected: (1) F/T measurement data, (2) Clinical Scale Description, (3) Natural Language Descriptions. This data will be collected for each patient during a number of visits in a six month period. According to the unsupervised approach that will be followed the information occurring for the data sets (2) and (3) will not influence the process of data set (1). Only at the final stage, after the completion of statistical analysis on data set (1) and the generation of the clusters and the definition of markers and milestones, will there be a procedure for associating them with the Natural Descriptions and if possible with Clinical Scales.

The following diagram summarises the stages/processes that should be followed during data processing and knowledge discovery in ALLADIN.

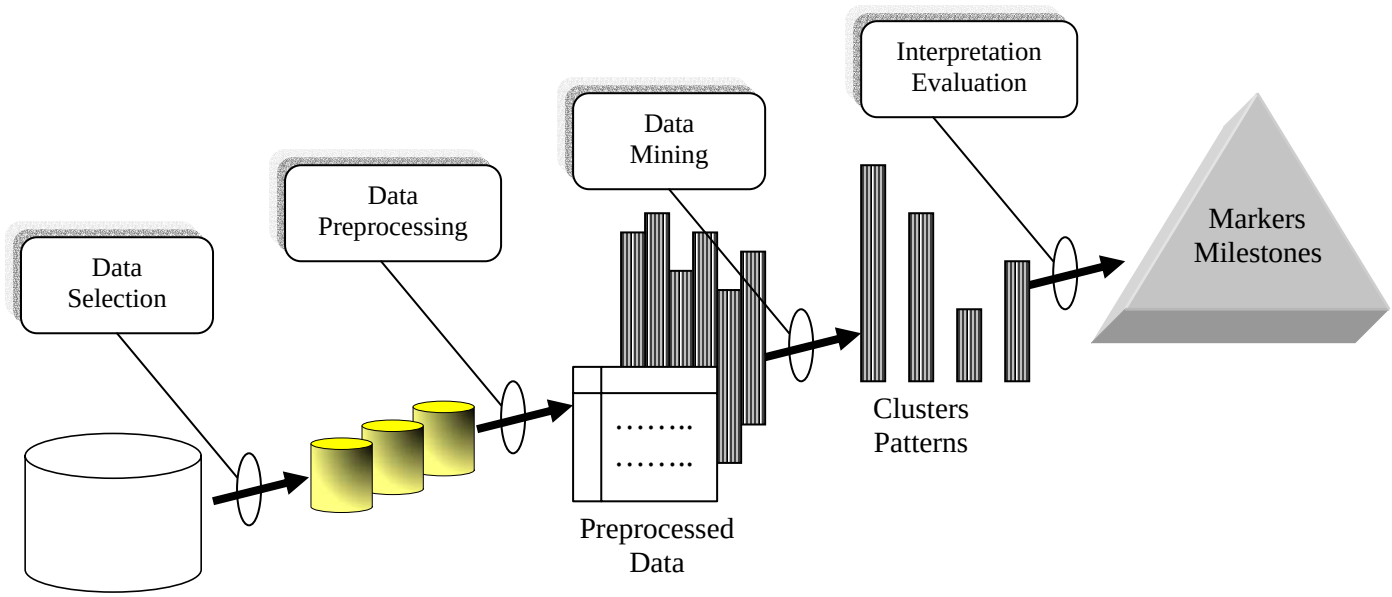


Figure 88 Data Statistical Process

The phases depicted start with the raw data and finish with the extracted information, markers and milestones, which were acquired as a result of the following stages: data selection, data preprocessing, data mining and interpretation. These stages are described in more detail in the following sections.

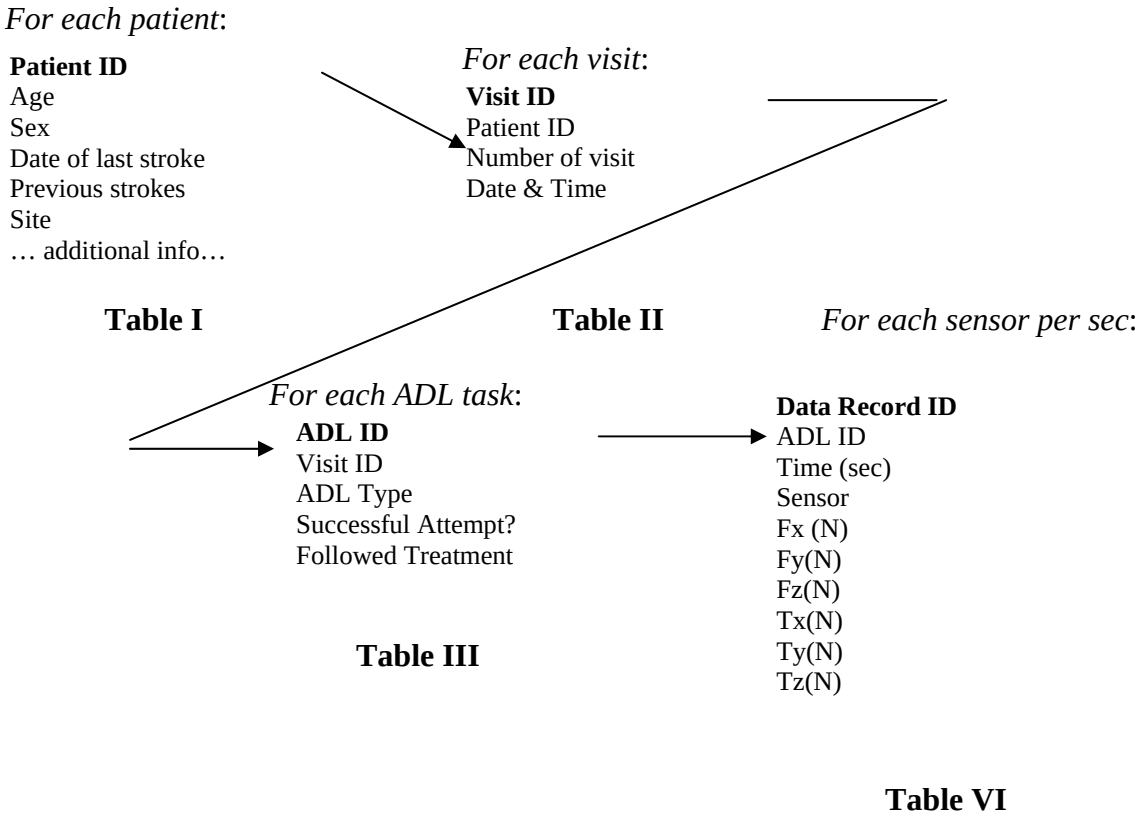
Data Selection

The aim is to select or segment the data according to some criteria. In order to be able to produce valuable results we can use, apart from the isometric F/T measurements data, some other information that may influence the patients' state. For example different demographic information or different treatments may conceal important information for one patient state. On the other hand, the successful or unsuccessful completion of an ADL task may affect the measured forces. Preferably, we should try different scenarios of data selection, examine the results produced for each scenario and, evaluate them.

In the following tables we tried to describe the information which we believe is important for our data mining procedures.

F/T Measurements from 3 sites

Targeted



Some of the data fields shown above may need further analysis (i.e. "Previous Strokes" in Table I, "Followed Treatment" in Table III). It is feasible that additional information, such as clinical patient data, would also be gathered. This data may or may not be used, but if it is not gathered the possibility of using it will not be an option. Additional information on measurement standards can be used as reference points.

Data Preprocessing

On a given set of data, preprocessing tasks should be applied to improve the quality of the results of data mining techniques. These tasks may be grouped in the following categories:

Data Cleansing

Data cleansing is done to ensure the data is accurate, reliable, complete and consistent. In ALLADIN, some data can be corrupted due to failure of the sensors and noise in the communication channel. Noise is random error or variance in a measured variable. Incorrect attribute values in the ALLADIN project may be due to faulty operation of instruments, probably as a result of the use of electronic circuits (white noise).

At this stage certain information is removed which is deemed unnecessary and may slow down queries. Outliers are also identified and noisy data is smoothed out. It is worth mentioning that the outlying data found must be treated carefully, and should be examined by domain experts.

There are in general two approaches when dealing with a data set containing noise. The first is to let the data modeling techniques be tolerant of the noise in the data. For

example, grid-based methods simply rely on input thresholds to eliminate low-populated cells. The second approach is to identify and eliminate the noisy data. Several methods have been developed in statistics for detecting noise. These methods usually measure the distance between the noisy data and the mean value of the whole data set and use some statistical significance test to see whether these noisy values are really from the same population. The disadvantage of this method lies in the fact that it can only deal with numerical data.

We may handle noisy data using:

- Binning methods
- Clustering
- Combined computer and human inspection
- Regression

Data Transformation

At this stage the data is made useable and navigable. The implementation of different data mining techniques and algorithms may need different data formulations. For data transformation several techniques may be applied:

- Smoothing
- Aggregation
- Generalization
- Normalization
- Attribute/feature construction

Data Reduction

At this stage we may test any possible correlations between the data and proceed accordingly, in order to obtain reduced representation in volume that produces the same or similar analytical results. Most popular reduction strategies are:

- Data cube aggregation
- Dimensionality reduction
- Numerosity reduction
- Discretization and concept hierarchy generation

Data Mining

This stage is concerned with the extraction of patterns from the data. A pattern can be defined as given a set of facts (data) F, a language L, and some measure of certainty C. A pattern is a statement S in L that describes relationships among a subset Fs of F with a certainty C such that S is simpler in some sense than the enumeration of all the facts in Fs.

For data mining we will use cluster analysis (clustering), an unsupervised learning approach. Clustering is the process of creating a partition so that all the members (data-objects) of each set of the partition are similar according to some metric. A cluster is a set of objects grouped together because of their similarity or proximity. Objects are often decomposed into an exhaustive and/or mutually exclusive set of clusters. Clustering is referred to as a procedure of unsupervised learning, because it is not based on predefined classes, unlike classification procedure (supervised learning) which requires the user to define one or more classes.

Different methods of clustering can be categorised according to:

- data types representing the objects
- ways of representing the clusters
- ways of organizing the clusters (hierarchical partitional, density-based, grid-based)
- algorithms that they use (Statistical, Conceptual, Kohonen Net, Fuzzy)

In an unsupervised learning environment the system has to discover its own classes and one way in which it does this is to cluster the data-objects in the database as shown in the following diagram (Fig. 3). The first step is to discover subsets of related objects and then find descriptions e.g. D1, D2, D3 etc. which describe each of these subsets.

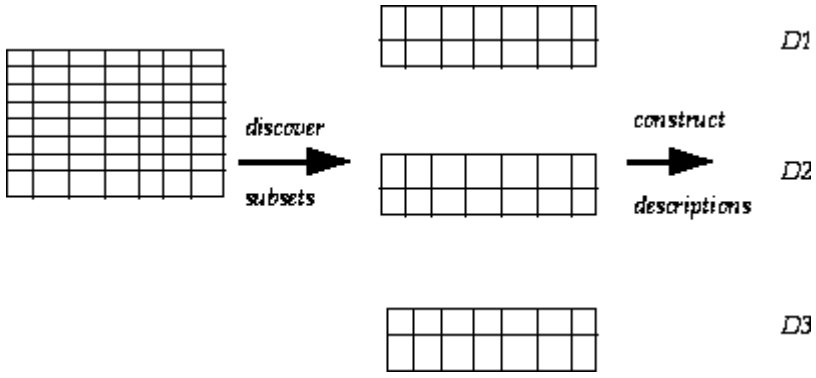


figure 89 Cluster Analysis

Clustering and segmentation basically partition the database so that each partition or group is similar according to some criteria or metric. Clustering according to similarity is a concept which appears in many disciplines. If a measure of similarity is available there are a number of techniques for forming clusters.

In our case, different clusters will represent different patients' states and from the clusters' descriptions we will try to discover markers and milestones. We will do this by finding attributes that present significant change between adjacent clusters.

In the ALLADIN project the data-objects that we are going to cluster are not the patients but the states of patients as each state is described by F/T data at every visit. Furthermore, it might be better to consider the different states of a patient as time-series data. Two approaches for dealing with time-series data are possible. First, these data can be transformed in a pre-processing step into the standard format of the general data mining algorithms. [127] This method greatly increases the dimensions of the problem. Second, a sequence discovery algorithm can be applied directly to the time-series data [76] [82] [119].

Here is a list of some popular algorithms grouped in four different categories based on the way of organizing the produced clusters:

Partitional

- K-Means
- K-Medoids (algorithms, PAM, CLARA, CLARANS, and its extension)
- Probabilistic clustering (algorithms, EM, SNOB, AutoClass, MCLUST)
- FCM (Fuzzy C-Means)

- FKM (Fuzzy K-Means)

Hierachical

- Single – Link (SL)
- Compltete – Link (CL)
- BIRCH
- CURE
- ROCK

Density-Based

- DBSCAN
- DENCLUE

Grid-Based

- Wave-Cluster
- STING

Another category of algorithms that we should consider and evaluate is this of Artificial Neural Networks (ANNs). Self-Organising Map (SOM) is an example of the algorithms in this category.

Methods that produce meaningful descriptions of clusters should be also considered. This is explained as follows. Clustering is usually viewed as a process of partitioning a collection of objects into groups of similar objects, according to some numerical measure of similarity. Such an approach to clustering has several limitations.[84] One is that clusters determined as groups of objects that are “close” to each other in a fixed, a priori assumed attribute space may lack any simple conceptual interpretations. Another important limitation of conventional methods is that they do not produce any conceptual description of the clusters. The problem of cluster interpretation is simply left to the data analyst. This is a serious drawback because data analysts are typically interested not only in determining clusters but also in formulating meaningful descriptions of them. Two approaches can be considered to obtain meaningful descriptions of clusters. First, conceptual or model-based clustering methods such as CLUSTER/2 [84] or COBWEB [42] can be utilised. In the CLUSTER/2 method, objects are arranged into classes representing certain descriptive concepts, rather than into classes defined solely by a similarity metric in some a priori defined attribute space. In the COBWEB method, each cluster is considered as a model that can be described intrinsically, rather than a collection of points assigned to it. Second, Clustering can be considered as a first step in data mining analysis. It identifies groups of related records that can be further explored. For example, rather than focus on each instance in the database, instances can be clustered first, and each cluster can be summarised and represented by its statistics, such as its mean, deviation etc. Subsequent analysis can be based on this compressed representation. Inductive learning algorithms can also be applied to each cluster to discover the patterns it possesses.

Another approach could be Markov Chains modeling. Indeed the transitions between different states of each patient are a kind of dynamic process and may be modeled as Markov Chains. After an initial study on this subject we conclude that we cannot use Markov Chains initially for discovering the clusters (different states), because we do not have the necessary information, as for example a pre-specified number of the states, nor the initial state distribution, nor the transition probabilities in the transition matrices. Nevertheless, we may try to model our problem as a Markov Chains Process and then apply agglomerative-metric

clustering procedures to discover the most probable set of clusters capturing different dynamics A Bayesian method for clustering is proposed in [104]. A new metric formally analogous to the correlation matrix for a Markov chain is proposed in [85].
Clustering algorithms are mostly metric-based, and typically the chosen metric is Euclidean. While easy to compute, Euclidean distance fails to incorporate local features of the data such as density, shape, and scale. Consequently, Euclidean-based algorithms perform poorly on data sets composed of clusters which are non-convex, randomly-oriented, or obscured by noise. So, at a latter state, after an initial metric-based clustering, we may use Markov chain approaches (i.e. HMM-Hidden Markov Models, EM algorithms) to improve the quality of the results. A probabilistic method for clustering discrete Markov processes with a pre-specified number of clusters is described in [106]

Interpretation and evaluation

During the final stage the patterns identified by the system are interpreted into knowledge which can then be used to support human decision-making. In our case, different clusters will represent different patients' states and from the clusters' descriptions we will try to discover markers and milestones. We will do this by finding attributes that present significant change between adjacent clusters.

Milestones and markers are often used as synonyms in the literature. The distinction between marker and milestone in ALLADIN is the following:

- A marker is considered as a sign that something is changing. It can be in the good or bad sense. In ALLADIN it is a synonym for predictor.

- A milestone is considered as a reached state. For example 'the patient can pick up a cup', however if he does it with an abnormal flexed wrist, the later is a marker for NO further development to fine finger control.

Finally, the milestones and the markers will be associated with Natural Language Descriptions and Clinical Scales. This association, at a final stage, will be integrated in the Clinical Standardization software.

Data Mining / Statistics Tools

The best way to assure the quality of the produced results is to try several different techniques, scenarios and algorithms for data preprocessing and data mining, before selecting the most appropriate.

According to DoW, we have to develop a set of software tools for implementing the data mining tasks. We have three alternatives:

- We may use as software components any of the popular Data Mining / Statistics Suites (SPSS (Celementine), DataEngine, SAS, MS SQL Server, etc)
- We may use tools that have been developed by MEC or any other partner (if any)
- We may develop a new set of tools using existing libraries of algorithms (such as those developed by the MEC).

After considering all the relevant aspects we will decide on the most appropriate scenario for developing a powerful and flexible software tool which will support the search for useful results.

Preliminary Study

The general conclusion from the design phase is that there are several points in the data processing task that should need further studying. There are a great variety of methods and algorithms that can be applied for data preprocessing, data mining and at the same time these algorithms may be applied through different software approaches. Before beginning the actual process of the collected data, during the 14th month of the project, we should follow a well defined procedure that will bring the necessary knowledge in a documented way. This knowledge should be our reference point for selecting these methods, algorithms and tools that we should focus on and test them with real data, towards the seeking of quality results.

In this procedure MEC, SSSA and ZENON shall undertake an active role and study thoroughly all the different approaches and produce the necessary documentation that will present advantages and disadvantages, past experience in relevant fields, compatibility with our set of data or any other useful information. For this documentation, reports using special format will be developed so that the information can be presented in a unified way.

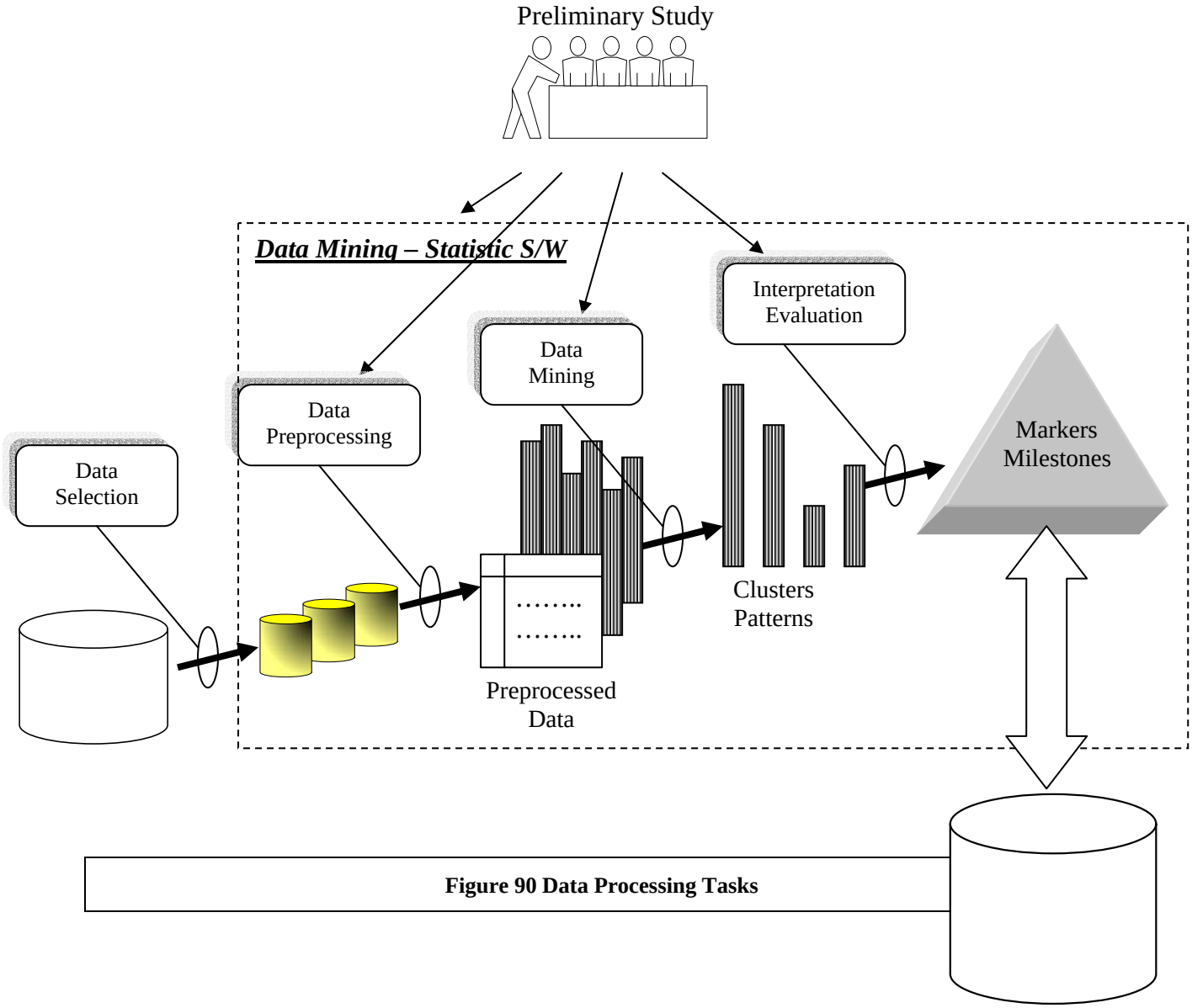


Figure 90 Data Processing Tasks

The results of this preliminary study will be a list of methods and algorithms that will be applied for data processing. The software tools that will be used for this purpose will be also defined. A representation of the whole procedure is shown in Figure 4.

5.5. Data Storage[7] [8]

5.5.1. The data storage architecture

The design of the database has an important factor on the performance of the application. Therefore several aspects must be considered, such as the type and size of the data, the way of data access, and many other features.

[7] EN 540:1993 Clinical investigation of medical devices for human subjects
[8] 95/46/EEC- COUNCIL DIRECTIVE 95/46/EEC of 24 October 1995 concerning personal data protection

The following data of the measurements are stored in the database:

- Patient data and case history
- Standard Outcome Measure (SOM)
- Natural language description of the patient status
- Voice records of the descriptions
- Force/torque measurement records of the ADL exercises

Other aspects

- The data is collected at three geographically distant clinical sites (at Budapest NIMR, Dublin TCD and Gent AHS)
- The clinical trial lasts for 18 months, in full working time (5 days, and 6 to 8 hours a week depending on the country).
- Large F/T measurement and sound files are recoded (several MB-s per records)
- The data is processed at some other sites, using statistical, data mining, and NLU technologies (at L&C, MEC, Multitel, SSSA and Zenon).
- This analysis operation requires intense database access.
- All these information processing partners need the entire database of the three clinical sites.

The database replication

The Alladin application is a distributed database solution with database replication.[9] [10] Replication is a solution for a distributed data environment when it is required to:

- Copy and distribute data to one or more sites.
- Distribute copies of data on a scheduled basis.
- Distribute data changes to other servers.
- Allow multiple users and sites to make changes then merge the data modifications together, potentially identifying and resolving conflicts.
- Build data applications that need to be used in online and offline environments.

Replication is the process of copying a database so that two or more copies can exchange updates of data or replicated objects. This exchange is called synchronization, which can be described as the process of updating two members of a replica set by exchanging all updated records and objects in each member. Two replica set members are synchronized when the changes in each have been applied to the other.

Replication topology

The replication topology defines the relationship between servers and the copies of data, along with the logic that determines how synchronization occurs between these copies. Replication could be a very complex issue, but in the case of the Alladin application we have a very simple situation:

- There is one global database.
- There are several local databases, which have a “parent/child” relationship with the global database.

[9] http://msdn.microsoft.com/library/default.asp?url=/library/en-us/replsql/replintro_5ir2.asp, Microsoft Developer Network, MS SQL Server 2002.
[10] http://www.dbmsmag.com/9705d15.html : Database replication, 1997 Miller Freeman

In this “parent/child” relationship, the “children” communicate only with the parent, namely the single global database, which contains all information, so there are no problems with simultaneous copies, and multiple paths.

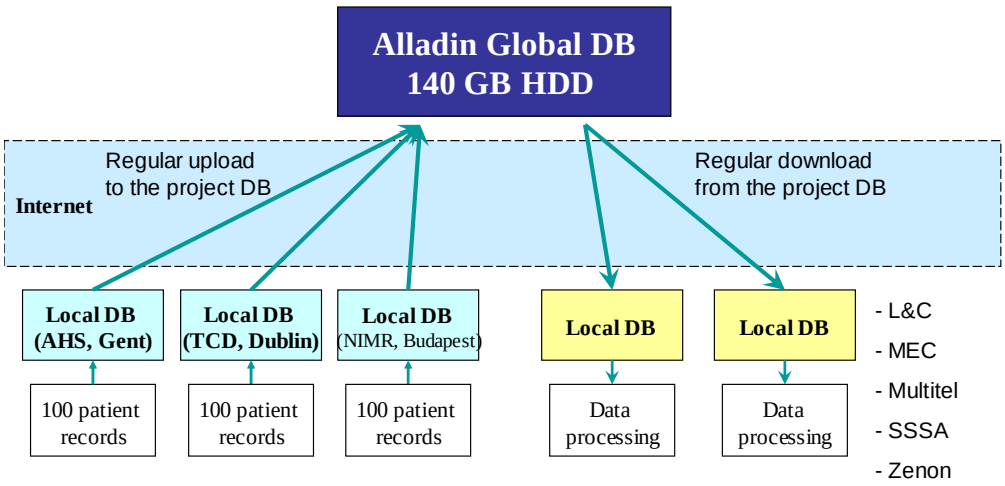


Figure 91. Data storage architecture

Figure 91 illustrates the architecture of the data storage and, the data flow, between the project participants. There are three sets of database, which are listed in the order of the data flow:

- **Databases at the clinical sites.** There are three clinical sites, where the patient data, and SOMs, biomedical measurements, and the clinical description are collected and stored.
- **Central project database.** This is the global database, where all measurement data from the clinical investigation is stored.
- **Databases at the information processing partners.** The data is finally processed at five different locations.

All these sites are interconnected via the Internet, therefore it is an obvious solution to synchronize the databases this way. The method of synchronization is described in chapter 5.5.5.

5.5.2. Local database at the clinical sites

The role of the database at the clinical sites is to store measurements during the clinical investigation, and transfer this data to the global database. Technically it is the local replica of the global project database.

There are two data sources (Figure 92) for the local database: the Alladin Measuring Application that provides the F/T data, and the PDA with the voice records and the SOM scores. The new patient data records are also created by the measuring application. The measurements are expected to take place during the full working day. Data records are mostly inserted into the database, but the clinicians may retrieve information on the patients’ previous treatments.

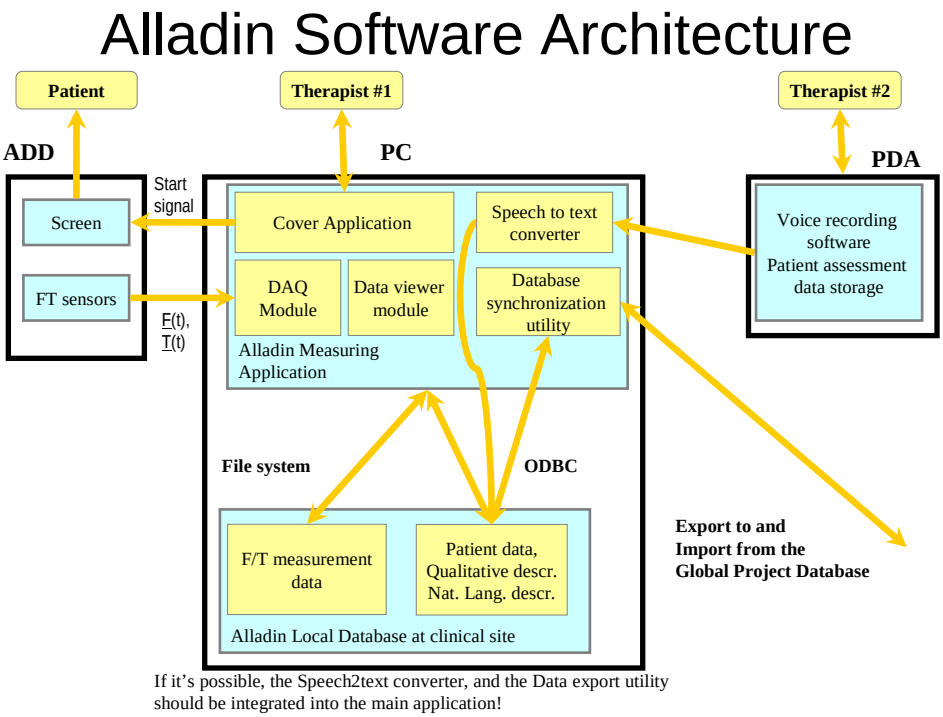


Figure 92. The place and role of the database in the Alladin application

The data at the clinical sites is stored in two logical units:

- A *SQL relational database*, and
- a *set of independent data files* on the hard disk, in a defined directory.

Naming conventions:

Each local database has its own identifier – the short name of the partner – which must be set, when the database is installed. This *PlaceID* is then used for synchronization, and also for consistent patient naming, in case of the clinical sites:

PlaceID	Description
AHS	Patients in AHS, Gent
NIMR	Patients in NIMR, Budapest
TCD	Patients in TCD, Dublin

Patient naming convention:

<PlaceID>-<number>

For example: AHS-003 is used for the third patient in AHS.

The SQL relational database

In case of a relational database, the different kinds of data are stored in tables, and the relationships between the tables are well defined. A relationship is an association established between common fields (columns) in two tables. Figure 93 shows the tables and relationships in the ALLADIN DB.

SQL is an acronym for Structured Query Language, and it is an international standard for describing the language of the databases. The ALLADIN local data storage is done in a *Microsoft Access Database*, which has an ODBC interface to external applications. In this way external applications can retrieve, insert, or modify data within the database using the SQL language.

The following data is stored in the relational database:

- Patient data and case history (see appendix for details)
- SOM
- Natural language description of the patient status

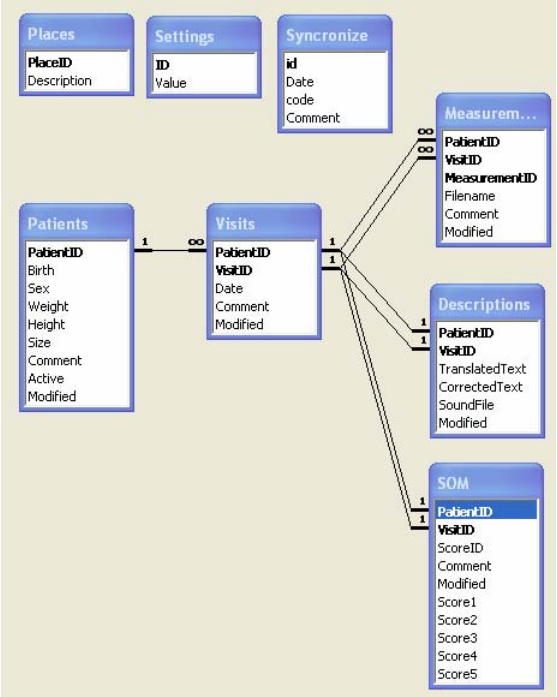


Figure 93. The Alladin relational database

Data stored in the set of independent files

Although technically possible, it is not usually advisable to store large data fields in a relational database, when the data is frequently accessed, because it can significantly reduce performance. In other words, it increases the access time of a data record. (Not to mention that MS Access mdb files have a 2GB size limit, which is also an overall database storage size, because all tables are stored in a single file. This limit would be exceeded at the clinical sites.) Therefore the oversized parts of the data are not included in the local relational database but instead, stored in external files.

These are:

- The *voice records* of the patient status descriptions.
- The *measurement data* of the ADL exercises. The force/torque trajectory patterns of several ADL exercise data are recorded for every measurement, approximately1 MB per ADL.

The relationship between the data files and the database is established by the *name of the file*.

Voice records:

The content of the voice file is a medium quality mono channel 8 bit sound file, in PCM format. One voice description is recorded per every patient measurement. The size of one file is estimated to be approximately 5MB.

Filename convention: <*PatientID*>-V<*VisitID*>.wav

E.g. the voice records of the *third* visit of patient called *AHS-005* is as follows:

PatientID	VisitID	Filename
AHS-005	3	AHS-005-V3.wav

F/T measurements of a single ADL:

The measurement files contain the binary representation of the F/T values as a function of the time called the F/T trajectory pattern. In the current configuration there are eight 6 axes F/T sensors in the diagnostic device giving a total of 8x6 = 48 measurement channels. The sample time is expected to be approximately 100Hz. Considering 32 bit representation of one F/T value (either fixed point, or floating point), and about 4 sec measurement cycles, the size of one ADL exercise measurement record is about 1300 kB. The size of the measurement files is shown in Figure 94.

Time [ms]	**Ch1 [N]**	**Ch2 [N]**	**Ch3 [N]**	**Ch4 [Nm]**	**Ch5 [Nm]**	**…**	**Ch48 [Nm]**
0	3	15	13	120	11	…	
10	…						
20							
…							

Figure 94. Table representation of the measurement data

filename convention: <*PatientID*>-V<*VisitID*>-M<*MeasurementID*>.wav

E.g. the *second* ADL exercise of the *third* visit of patient called TCD-*005* is than:

PatientID	VisitID	MeasurementID	Filename
TCD-005	3	2	TCD-005-V3-M2.wav

Database size

Figure 95 illustrates the size of the individual components (the SQL database, the FT data records, and the voice records) in the local and global databases. The voice records occupy the largest space.

Description	record count	Relational DB	FT data	voices	DB+Ftdata +voices
Global Project DB [MB]	**1 x**	**41**	**107 578**	**51 000**	**158 620**
Local DB at clinical sites [MB]	**3 x**	**14**	**35 859**	**17 000**	**52 873**
Patient Records [MB]	100 x	0	359	170	529
Patient physical data [MB]	1 x	0.001			0.001
Case history [MB]	1 x	0.001			0.001
Clinical assessments - SOM [MB]	34 x	0.001			0.001
Natural language descriptions [MB]	34 x	0.003			0.003
Voice records [MB]	34 x			5.000	5.000
F/T data of one visit [MB]	**34 x**		**10.547**		**10.547**
compression ratio			1		1
Raw F/T data [MB]			10.547		10.547
number of channels			48		48
frequency [Hz]			100		100
measurement time [sec]			576		576
size of one sample [Byte]			4		4

Figure 95. Size of the database components

5.5.3. The central project database

The role of the central project database is as follows:

- It is a global copy of the database, and all the data is stored here by means of DB synchronization.
- It provides an ODBC interface to access, and modify the database. (The logic of database synchronization is implemented in the client side at the clinical sites and the information processing partners.)
- Regular system backup provides data protection, thus a system failure at a clinical site can be recovered fully from this central database.

Relational database

There is a "parent/child" relationship between this central project database, and the clinical databases. All other database instances are local replicas of this global database. The synchronization is described in chapter 5.5.5.

The entire database is stored in a MySQL database (MySQL database server v4.0.18). The same tables are stored in the database, as in the local databases. This database implementation is capable of storing and managing extremely large data tables, so technically it is possible to store the large binary files either in the database or external files.

The MySQL server – unlike Microsoft Access's mdb files – stores the data tables in separate files, and on the other hand the global database is not accessed frequently, only at the database synchronization, so it does not decrease the performance significantly to store the large binary files inside the database. However it is a more consistent way to store everything in one storage unit. Notwithstanding, it could be reasonable to store the binary data files in external files, because in this way an other file transfer system (like SSH2 protocol) could be used. The SSH2 protocol enables file compression on a connection, thus the upload time could be reduced.

Web-interface to the database

There is a simple web front-end of the Alladin project database – developed in PHP. The main page of the provisional prototype can be found at http://frontinus.manuf.bme.hu/~jurak/db/ during the development phase, but finally it will be integrated to the ALLADIN homepage. In this page the content of the database tables can be displayed with some simple filtering. It is easy to look up e.g. a specific visit of a certain patient.

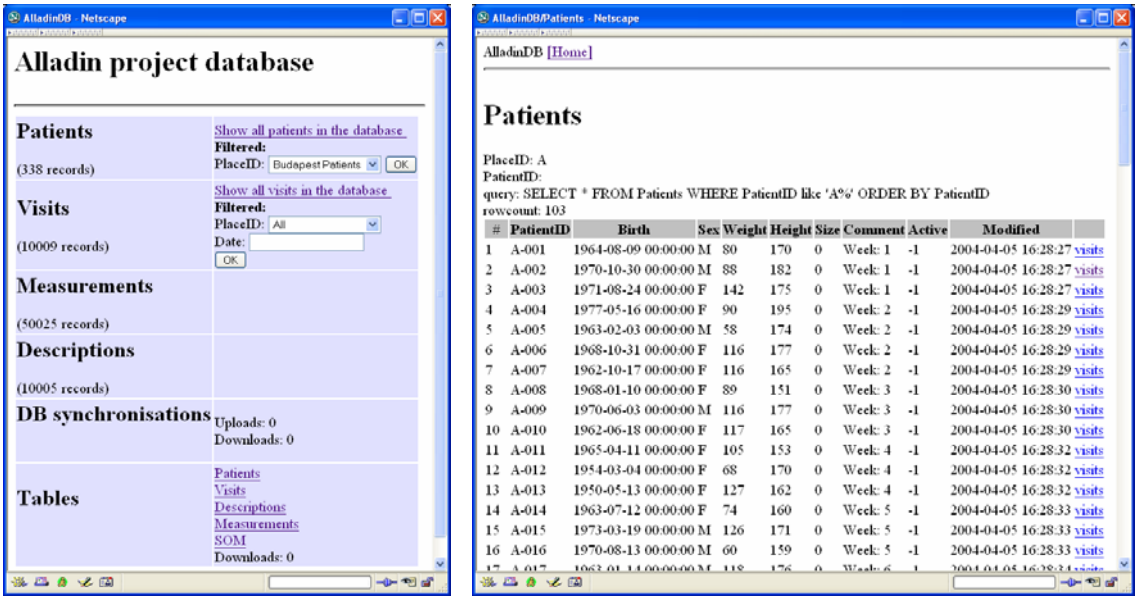


Figure 96. Simple web front end to the database

Web-access provides a means for either the clinical or data processing partners to check the actual content of the database. Later other sophisticated reporting, and checking functions can be implemented, if it is required by the clinical or data processing partners. It will be located in the secure area of the ALLADIN homepage, which is not accessible to project outsiders.

5.5.4 Local storage at the information processing partners

The role of this database is to provide all data, which has been recorded by the clinical sites, to the data processing partners. They are extracting some extra relationships between the measured data and the patient's status, using data mining, statistical, and NLU technologies. Technically it is the same local database like at the clinical sites, only the PlaceID is different. However its content is obtained in full from the central project database by the means of database synchronization, no measurements are made at the information processing partners.

5.5.5 Replication (Database synchronization)

The need for replication is described in previous chapters. Here the brief technical implementation is described, how each local database replica is synchronized to the global database. By the term 'synchronization' we mean *data exchange* of the replica set between two members.

Method of synchronization

The Global and local databases are designed to be able to be synchronized, that is to identify and transfer the new records and modified data to the other database. Synchronization operation is always initiated and performed by the local DB. The logic of synchronization is implemented at the client side.

The following operations are required to exchange data:

- Update the global database:
  - Copy new data records from the *local DB* to the *global* tables.
  - Update those records in the *global DB*, which has been modified in the *local DB*.
- Update local database
  - Copy new data records from the *global DB* to *local* tables.
  - Update those records in the *local DB*, which has been modified in the *global DB*.

The clinical sites only upload data to the server, while the information processing partners only download the data from the server.

All replicated tables have a unique key, which uniquely identifies a record of data. The new records are identified by these unique keys. The modification could be traced in two ways:

- By consistent usage of a date-type *modify* column in each record, which is updated with the current date automatically, when the data record is modified. The value of this column could be compared to the other database's record, and the older records should be updated with the newer. The drawback of this method is that we rely on the system time of the client computers.
- By consistent usage of a flag-type *modified* column in each record. When a record is modified at a clinical site, it sets the *modified* flag for that record. At the next synchronization the content of this record updates the global database, and the flag is

cleared. In this case we can utilize the nature of data flow, and do not rely on system times.

Replication time and schedule

Depending on the final size of the data records and the internet connection speed, the synchronization will take several minutes. The following table summarizes the calculated theoretical time for synchronization:

Description		Daily update with dialup	Daily update with DSL	Daily update with DSL 512	Weekly update with dialup	Weekly update with ISDN	Weekly update with DSL	Weekly update with DSL 512	Weekly update with DSL 1024
Required time	**[min]**	**357**	**78**	**39**	**1786**	**781**	**391**	**195**	**98**
Connection speed	**[kbps]**	**56**	**256**	**512**	**56**	**128**	**256**	**512**	**1024**
Connection speed	[kBps]	7	32	64	7	16	32	64	128
Size of one mesurement	[MB]	15	15	15	15	15	15	15	15
measurements per day		10	10	10	10	10	10	10	10
Upload period	[days]	1	1	1	5	5	5	5	5
Upload size	**[MB]**	**150**	**150**	**150**	**750**	**750**	**750**	**750**	**750**

Figure 97 Theoretical synchronization time requirements with different connection speeds.

Some elements of the synchronization may not take place concurrently. Thus, to avoid synchronization conflicts, we propose the following schedule:

- clinical sites are synchronized once a week to the global database at a fixed time.
- Information processing partners are not modifying the content of the data records at the global database; therefore it is not a problem to synchronize multiple instances of such databases concurrently. These partners could synchronize their databases at any other time to the global DB (CET).

Concurrent access attempts are automatically handled by DB *locking* mechanism. In case of prohibited access, the DB access operation results with an access denied error, so the synchronization operation could not even start at a second local DB client, until the lock is released by the first client.

The schedule is presented in the table, below. All afternoons are reserved for the clinical partners for synchronization. The three partners are scheduled from Wednesday to Friday, one partner per day. In case of a network breakdown, or other synchronization failure, Monday and Tuesday afternoons are also reserved for them. In the remaining time the information processing partners are free to access and synchronize their local database. They can do this on a daily or weekly basis, but we propose a weekly synchronization schedule for them on Monday mornings.

Time CET	Monday	Tuesday	Wednesday	Thursday	Friday	Weekend
0:00-15:00	Information processing partners					
15:00-17:00	*Reserved for clinical*	*Reserved for clinical*	Reserved for AHS	Reserved for NIMR	Reserved for TCD	

	Sites	*Sites*				
17:00-24:00						

Appendix

ALLADIN project DATA ENTRY

Date of admission
Date of discharge
Case ID
Participant No

DEMOGRAPHIC INFORMATION

NAME FIRST _____ FAMILY_____

SEX [ ] Female [ ] Male

DATE OF BIRTH _ _/_ _/_ _ *(date/month/year)*

ADDRESS

CURRENT MARITAL STATUS: *(Check only one that is most applicable)*

Never married [ ]
Divorced [ ]
Currently Married [ ]
Widowed [ ]
Separated [ ]
Cohabiting [ ]

CURRENT OCCUPATION *(Select the single best option)*

Paid employment [ ]
Self-employed [ ]
Non-paid work, such as volunteer/charity [ ]
Student [ ]
Keeping house/House-maker [ ]
Retired [ ]
Unemployed (health reason) [ ]
Unemployed (other reason) [ ]
Other [ ]

MEDICAL DIAGNOSIS of existing Main Health Conditions, *if possible give ICD Codes.*

No Medical Condition exists [ ]
…….. ICD code: __. __. __.__. __

…….. ICD code: __. __. __.__. __
…….. ICD code: __. __. __.__. __
A Health Condition (disease, disorder, injury) exists, however its nature or diagnosis is not known [ ]

IMPAIRMENTS of BODY FUNCTIONS

Body functions are the physiological functions of body systems (including psychological functions). Impairments are problems in body function as a significant deviation or loss.

Qualifier:
0 No impairment,
1 Mild impairment,
2 Moderate impairment
3 Severe impairment
4 Complete impairment
8 Not specified
9 Not applicable

b1. MENTAL FUNCTIONS
b110 Consciousness
b114 Orientation *(time, place, person)*
b117 Intellectual *(incl. Retardation, dementia)*
b130 Energy and drive functions
b134 Sleep
b140 Attention
b144 Memory
b152 Emotional functions
b156 Perceptual functions
b164 Higher level cognitive functions
b167 Language

b2. SENSORY FUNCTIONS AND PAIN
b210 Seeing
b230 Hearing
b235 Vestibular *(incl. Balance functions)*
b280 Pain

b3. VOICE AND SPEECH FUNCTIONS
b310 Voice

b4. FUNCTIONS OF THE CARDIOVASCULAR, HAEMATOLOGICAL, IMMUNOLOGICAL AND RESPIRATORY SYSTEMS
b410 Heart
b420 Blood pressure
b430 Hematological *(blood)*
b435 Immunological *(allergies, hypersensitivity)*
b440 Respiration *(breathing)*

b6. GENITOURINARY AND REPRODUCTIVE FUNCTIONS
b620 Urination functions - Incontinence

b7. NEUROMUSCULOSKELETAL AND MOVEMENT RELATED FUNCTIONS
b710 Mobility of joint
b730 Muscle power
b735 Muscle tone
b765 Involuntary movements

IMPAIRMENTS of BODY STRUCTURES

Body structures are anatomical parts of the body such as organs, limbs and their components. Impairments are problems in structure as a significant deviation or loss.

First qualifier: Extent of impairment	Second qualifier: Nature of change	Third qualifier: location
0 No impairment	**0** No change in structure	**0** More than one region
1 Mild impairment	**1** Total absence	**1** right
2 Moderate impairment	**2** Partial absence	**2** left
3 Severe impairment	**3** Additional part	**3** both sides
4 Complete impairment	**4** Aberrant dimensions	**4** front
8 Not specified	**5** Discontinuity	
9 Not applicable	**6** Deviating position	**5** back
	7 Qualitative changes in structure, including accumulation of fluid	**6** proximal
	8 Not specified	**7** distal

s1. STRUCTURE OF THE NERVOUS SYSTEM
s110 Brain
s120 Spinal cord and peripheral nerves
s2. THE EYE, EAR AND RELATED STRUCTURES
s3. STRUCTURES INVOLVED IN VOICE AND SPEECH
s4. STRUCTURE OF THE CARDIOVASCULAR, IMMUNOLOGICAL AND RESPIRATORY SYSTEMS
s410 Cardiovascular system
s430 Respiratory system
s5. STRUCTURES RELATED TO THE DIGESTIVE, METABOLISM AND ENDOCRINE SYSTEMS
s6. STRUCTURE RELATED TO GENITOURINARY AND REPRODUCTIVE SYSTEM
s610 Urinary system
s7. STRUCTURE RELATED TO MOVEMENT
s710 Head and neck region
s720 Shoulder region
s730 Upper extremity *(arm, hand)*
s740 Pelvis
s750 Lower extremity *(leg, foot)*
s760 Trunk
s8. SKIN AND RELATED STRUCTURES
ANY OTHER BODY STRUCTURES

ACTIVITY LIMITATIONS & PARTICIPATION RESTRICTION

Activity *is the execution of a task or action by an individual..* ***Participation*** *is involvement in a life situation.*

Activity limitations *are difficulties an individual may have in executing activities.*
Participation restrictions *are problems an individual may have in involvement in life situations.*

The Performance qualifier *describes what an individual does in his or her current environment. Because the current environment brings in the societal context, performance can also be understood as "involvement in a life situation" or "the lived experience" of people in the actual context in which they live. This context includes the environmental factors – all aspects of the physical, social and attitudinal world that can be coded using the Environmental Factors*

.

The Capacity qualifier *describes an individual's ability to execute a task or an action. This construct indicates the highest probable level of functioning that a person may reach in a given domain at a given moment. To assess the full ability of the individual, one would need to have a "standardized" environment to neutralize the varying impact of different environments on the ability of the individual. As standardized environment may be: (a) an actual environment commonly used for capacity assessment in test settings; or (b)where this is not possible, a hypothetical environment a uniform impact.*

Note: Use Appendix 2 if needed to elicit information on the Activities and Participation of the individual

First Qualifier: ***Performance***
Extent of Participation Restriction
0 No difficulty
1 Mild difficulty
2 Moderate difficulty
3 Severe difficulty
4 Complete difficulty
8 Not specified
9 Not applicable

Second Qualifier: ***Capacity (without assistance)***
Extent of Activity limitation
0 No difficulty
1 Mild difficulty
2 Moderate difficulty
3 Severe difficulty
4 Complete difficulty
8 Not specified
9 Not applicable

Short List of A&P domains	***Performance Qualifier***	***Capacity Qualifier***
d2. GENERAL TASKS AND DEMANDS		
d210 Undertaking a single task		
d220 Undertaking multiple tasks		
d3. COMMUNICATION		
d330 Speaking		
d350 Conversation		
d4. MOBILITY		
d430 Lifting and carrying objects		
d440 Fine hand use *(picking up, grasping)*		
d450 Walking		
d465 Moving around using equipment *(wheelchair, skates, etc.)*		

d470 Using transportation *(car, bus, train, plane, etc.)*
d475 Driving (riding bicycle and *motorbike, driving car, etc.)*

d5. SELF CARE

d510 Washing oneself *(bathing, drying, washing hands, etc)*
d520 Caring for body parts *(brushing teeth, shaving, grooming, etc.)*
d530 Toileting
d540 Dressing
d550 Eating
d560 Drinking
d570 Looking after one`s health

d6. DOMESTIC LIFE

d620 Acquisition of goods and services *(shopping, etc.)*
d630 Preparation of meals *(cooking etc.)*
d640 Doing housework *(cleaning house, washing dishes laundry, ironing, etc.)*
d660 Assisting others

BRIEF HEALTH INFORMATION

Height : __/__/__ cm *(or inches)*

Weight: __/__/__ kg *(or pounds)*

Dominant Hand *(prior to health condition)*:

Left [ ] Right [ ] Both hands equally [ ]

How do you rate your physical health in the past month?

Very good [ ] Good [ ] Moderate [ ] Bad [ ] Very bad [ ]

How do you rate your mental and emotional health in the past month?

Very good [ ] Good [ ] Moderate [ ] Bad [ ] Very bad [ ]

Do you currently have any disease(s) or disorder(s) ?

[ ] NO [ ] YES
*If YES, please specify:*_____

Did you ever have any significant injuries that had an impact on your level of functioning?

[ ] NO [ ] YES
If YES, please specify _____

Have you been hospitalized in the last year?

[ ] NO [ ] YES

If YES, please specify reason(s) and for how long?

1. _____; ___. ___. ___ days
2. _____; ___. ___. ___ days
3. _____; ___. ___. ___ days

Are you taking any medication (either prescribed or over the counter)?

[ ] NO [ ] YES

If YES, please specify major medications

1. _____
2. _____
3. _____

Do you smoke?

[ ] NO [ ] YES

Do you consume alcohol or drugs?

[ ] NO [ ] YES

If YES, please specify average daily quantity

Tobacco: _____

Alcohol: _____

Drugs: _____

Do you use any assistive device such as glasses, hearing aid, wheelchair, etc.?

[ ] NO [ ] YES

If YES, please specify

Do you have any person assisting you with your self care, shopping or other daily activities?

[ ] NO [ ] YES
If YES, please specify person and assistance they provide

Are you receiving any kind of treatment for your health?

[ ] NO [ ] YES
If YES, please specify:

Additional significant information on your past and present health:

IN THE PAST MONTH, have you cut back (i.e. reduced) your usual activities or work because of your *health condition*? (a disease, injury, emotional reasons or alcohol or drug use)

[ ] NO [ ] YES If yes, how many days? _____

IN THE PAST MONTH, have you been totally unable to carry out your usual activities or work because of your *health condition*? (a disease, injury, emotional reasons or alcohol or drug use)

[ ] NO [ ] YES If yes, how many days? _____

5.6. Interim reports

Interim reports refer to the evaluation of data from a clinical trial before its completion. The pharmaceutical industry has been performing interim analyses to prevent the exposure of patients to unreasonable risks or impose on them the burdens of a clinical trial without having a reasonable expectation that the trial would produce useful information. Similarly, the uncertainty about the efficacy of a new drug may result in a trial designed to accrue many more patients than are needed to demonstrate its therapeutic activity.

Interim analysis typically involves unblinding the patients' treatment assignment before all the trial data have been collected. Masking the treatment is an essential mechanism of bias

prevention. Thus, controlling the dissemination of preliminary results during an ongoing trial is a critical element of an interim analysis plan.

Two interim reports will be prepared during the ALLADIN clinical trial. The first report will be prepared when 70% of the trial is completed. The reason is to have sufficient data with even distribution of patient population because it exists a possibility that patients with similar profiles will participate in the beginning of the trial. This similarity may occur due to that the clinical trail will be conducted during a period of 14 month but each patient will take part for a duration of six months. The second report will be prepared when 85% of the trial is completed

5.6.1. Responsibility

The team (ZENON, MEC, SSSA) processing the data in order to find hidden pattern are responsible for producing and evaluating the interim reports. This might look like a contradiction to normal procedures that uses independent parties but in the ALLADIN context it is not. As already discussed in Section 3.2.Blinding, the aim of the ALLADIN trials is to detect hidden markers and milestones of recovery by analysing measurement data obtained from patients performing ADL tasks. The data processing team does not have knowledge of the physiotherapist's assessment of the patient and does not need this information in order to evaluate if the results derived from the data mining are of sufficient quality. In data mining techniques several indices may assess the statistical quality of the results.

5.6.2. Influence on protocol

In order to draw conclusion from the report and, if needed, propose changes to the trial protocol, the clinical partners will need to provide the data processing team with patient statistics concerning demographic characteristics and entering condition (in the form of clinical scale values), see 2.1.2.Over and Under Representation. For example, if satisfactory results have been obtained for the first interim report that might indicate that the trial could stop, but the patient statistics reveal that only patients covering 3/4 of a specific segment have so far taken part in the trial, then the conclusion might be to continue the trial but focus the patient selection to cover the rest 1/4 of the segment.

Reference List

[1] http://www.chattecx.com. 2004.
Ref Type: Internet Communication

[2] http://www.csmisolutions.com/isokinetic/main.shtml. 2004.
Ref Type: Internet Communication

[3] http://www.newtest.com. 2004.
Ref Type: Internet Communication

[4] http://www.ie.ncsu.edu/ergolab/equipment/b200.html. 2004.
Ref Type: Internet Communication

[5] http://jsc-web-pub.jsc.nasa.gov/hefo/hhfo/abf/dynamometers.asp. 2004.
Ref Type: Internet Communication

[6] http://www.biodex.com. 2004.
Ref Type: Internet Communication

[7] http://www.jr3.com. 2004.
Ref Type: Internet Communication

[8] Mannequin Pro, NexGen Ergonomics. 2004.
Ref Type: Internet Communication

[9] People size, Open ergonomics. 2004.
Ref Type: Internet Communication

[10] Annett J. Motor imagery: perception or action? Neuropsychologia 1995;33(11):1395-417.

[11] Bachman K. Using mental imagery to practice a specific psychomotor skill. J.Contin.Educ.Nurs. 1990;21(3):125-8.

[12] Barreca S, Wolf SL, Fasoli S, Bohannon R. Treatment interventions for the paretic upper limb of stroke survivors: a critical review. Neurorehabil.Neural Repair 2003;17(4):220-6.

[13] Beer RF, Given JD, Dewald JP. Task-dependent weakness at the elbow in patients with hemiparesis. Arch.Phys.Med.Rehabil. 1999;80(7):766-72.

[14] Beer RF, Dewald JP, Rymer WZ. Disturbances of voluntary movement in stroke: problems of planning or execution. Prog Brain Res 1999;123:455-60.

[15] Beer RF, Dewald JP, Rymer WZ. Deficits in the coordination of multijoint arm movements in patients with hemiparesis: evidence for disturbed control of limb dynamics. Exp.Brain Res. 2000;131(3):305-19.

[16] Beer RF, Dewald JP, Dawson ML, Rymer WZ. Target-dependent differences between free and constrained arm movements in chronic hemiparesis. Exp.Brain Res. 2004.

[17] Bobath B. Adult hemiplegia: evaluation and treatment. London: William Heinemann Medical Books; 1978.

[18] Bohan M, Pharmer JA, Stokes AF. When does imagery practice enhance performance on a motor task? Percept.Mot.Skills 1999;88(2):651-8.

[19] Brunstrom S. Movement therapy in hemiplegia: a neuro physiological approach. New York: Harper and Row; 1970.

[20] Buchanan TS, Moniz MJ, Dewald JP, Zev RW. Estimation of muscle forces about the wrist joint during isometric tasks using an EMG coefficient method. J.Biomech. 1993;26(4-5):547-60.

[21] Buchanan TS, Shreeve DA. An evaluation of optimization techniques for the prediction of muscle activation patterns during isometric tasks. J.Biomech.Eng 1996;118(4):565-74.

[22] Burgess PR, Jones LF, Buhler CF, Dewald JP, Zhang LQ, Rymer WZ. Muscular torque generation during imposed joint rotation: torque-angle relationships when subjects' only goal is to make a constant effort. Somatosens.Mot.Res. 2002;19(4):327-40.
[23] Carr J, Shepard R. Neurological rehabilitation. Oxford: Butterworth-Heineman; 1998.
[24] Chung SG, van Rey E, Roth EJ, Zhang LQ. Aging-Related Changes in Achilles' Tendon Reflexes. Arch.Phys.Med.Rehabil. 2003;84:E14.
[25] Clark S, Tremblay F, Ste-Marie D. Differential modulation of corticospinal excitability during observation, mental imagery and imitation of hand actions. Neuropsychologia 2004;42(1):105-12.
[26] Council directive 93/42/EEC. 93/42/EEC 14 June 1993 concerning medical devices. 1993. Ref Type: Report
[27] Cronbach LJ. Coefficient alpha and the internal structure of tests. Psychometrica 1951;16:297-334.
[28] Cunnington R, Iansek R, Bradshaw JL, Phillips JG. Movement-related potentials associated with movement preparation and motor imagery. Exp.Brain Res. 1996;111(3):429-36.
[29] Danckert J, Ferber S, Doherty T, Steinmetz H, Nicolle D, Goodale MA. Selective, non-lateralized impairment of motor imagery following right parietal damage. Neurocase. 2002;8(3):194-204.
[30] de'Sperati C, Stucchi N. Motor imagery and visual event recognition. Exp.Brain Res. 2000;133(2):273-8.
[31] Decety J. The neurophysiological basis of motor imagery. Behav.Brain Res. 1996;77(1-2):45-52.
[32] Deecke L. Planning, preparation, execution, and imagery of volitional action. Brain Res.Cogn Brain Res. 1996;3(2):59-64.
[33] Deutsch J, Latonio J, Burdea G, Boian R. Post-Stroke Rehabilitation with the Rutgers Ankle System - A case study. Presence 2001;10:416-430.
[34] Dewald JP, Pope PS, Given JD, Buchanan TS, Rymer WZ. Abnormal muscle coactivation patterns during isometric torque generation at the elbow and shoulder in hemiparetic subjects. Brain 1995;118 (Pt 2):495-510.
[35] Dewald JP, Beer RF, Given JD, McGuire JR, Rymer WZ. Reorganization of flexion reflexes in the upper extremity of hemiparetic subjects. Muscle Nerve 1999;22(9):1209-21.
[36] Dewald JP, Sheshadri V, Dawson ML, Beer RF. Upper-limb discoordination in hemiparetic stroke: implications for neurorehabilitation. Top.Stroke Rehabil. 2001;8(1):1-12.
[37] Dewald JP, Beer RF. Abnormal joint torque patterns in the paretic upper limb of subjects with hemiparesis. Muscle Nerve 2001;24(2):273-83.
[38] Ehrsson HH, Geyer S, Naito E. Imagery of voluntary movement of fingers, toes, and tongue activates corresponding body-part-specific motor representations. J.Neurophysiol. 2003;90(5):3304-16.
[39] Facchini S, Muellbacher W, Battaglia F, Boroojerdi B, Hallett M. Focal enhancement of motor cortex excitability during motor imagery: a transcranial magnetic stimulation study. Acta Neurol.Scand. 2002;105(3):146-51.
[40] Fery YA. Differentiating visual and kinesthetic imagery in mental practice. Can.J.Exp.Psychol. 2003;57(1):1-10.
[41] Fischer MH. Can we correctly perceive the reaching range of others?. Br.J.Psychol. 2003;94(Pt 4):487-500.
[42] Fisher. Knowledge acquisition via incremental conceptual clustering. Machine Learning 1987;2:139-72.

[43] Fugl-Meyer A, Jaasko AR, Leyman I, Olsson S, Steglind S. The post stroke hemiplegic patient. I. A method for evaluation of physical performance. Scand J Rehab Med 1975;7:13-31.
[44] Gandevia SC. Mind, muscles and motoneurones. J.Sci.Med.Sport 1999;2(3):167-80.
[45] Ghez C, Favilla M, Ghilardi MF, Gordon J, Bermejo R, Pullman S. Discrete and continuous planning of hand movements and isometric force trajectories 9. Exp.Brain Res. 1997;115(2):217-33.
[46] Given JD, Dewald JP, Rymer WZ. Joint dependent passive stiffness in paretic and contralateral limbs of spastic patients with hemiparetic stroke. J.Neurol.Neurosurg.Psychiatry 1995;59(3):271-9.
[47] Gordon D, Robertson E, Stephen D. Approaches to obtaining three dimensional information about biological systems. Ottawa Canada: 2004.
[48] Gresham GE, Kelly-Hayes M, Wolf PA, Beiser AS, Kase CS, D'Agostino RB. Survival and functional status 20 or more years after first stroke. stroke 1998;29:793-67.
[49] Grezes J, Decety J. Does visual perception of object afford action? Evidence from a neuroimaging study. Neuropsychologia 2002;40(2):212-22.
[50] Hale BS, Raglin JS, Koceja DM. Effect of mental imagery of a motor task on the Hoffmann reflex. Behav.Brain Res. 2003;142(1-2):81-7.
[51] Hall C, Buckolz E, Fishburne GJ. Imagery and the acquisition of motor skills. Can.J.Sport Sci. 1992;17(1):19-27.
[52] Hall JC. Imagery practice and the development of surgical skills. Am.J.Surg. 2002;184(5):465-70.
[53] Hamrin E, Wohlin A. Evaluation of functional capacity of stroke patients through an Activity Index. Scand J Rehab Med 1982;14:93-100.
[54] Hanakawa T, Immisch I, Toma K, Dimyan MA, Van Gelderen P, Hallett M. Functional properties of brain areas associated with motor execution and imagery. J.Neurophysiol. 2003;89(2):989-1002.
[55] Hashimoto R, Rothwell JC. Dynamic changes in corticospinal excitability during motor imagery. Exp.Brain Res. 1999;125(1):75-81.
[56] Herrmann U, Flanders M. Directional tuning of single motor units. J.Neurosci. 1998;18(20):8402-16.
[57] Hummelsheim H. Rationales for improving motor function. Curr.Opin.Neurol. 1999;12(6):697-701.
[58] Jackson PL, Lafleur MF, Malouin F, Richards C, Doyon J. Potential role of mental practice using motor imagery in neurologic rehabilitation. Arch.Phys.Med.Rehabil. 2001;82(8):1133-41.
[59] Jackson PL, Lafleur MF, Malouin F, Richards CL, Doyon J. Functional cerebral reorganization following motor sequence learning through mental practice with motor imagery. Neuroimage. 2003;20(2):1171-80.
[60] Jeannerod M. Mental imagery in the motor context. Neuropsychologia 1995;33(11):1419-32.
[61] Johnson SH. Imagining the impossible: intact motor representations in hemiplegics. Neuroreport 2000;11(4):729-32.
[62] Johnson SH. Thinking ahead: the case for motor imagery in prospective judgements of prehension. Cognition 2000;74(1):33-70.
[63] Johnson SH, Corballis PM, Gazzaniga MS. Within grasp but out of reach: evidence for a double dissociation between imagined hand and arm movements in the left cerebral hemisphere. Neuropsychologia 2001;39(1):36-50.

[64] Johnson SH, Rotte M, Grafton ST, Hinrichs H, Gazzaniga MS, Heinze HJ. Selective activation of a parietofrontal circuit during implicitly imagined prehension. Neuroimage. 2002;17(4):1693-704.
[65] Johnson SH, Sprehn G, Saykin AJ. Intact motor imagery in chronic upper limb hemiplegics: evidence for activity-independent action representations. J.Cogn Neurosci. 2002;14(6):841-52.
[66] Kaneko F, Murakami T, Onari K, Kurumadani H, Kawaguchi K. Decreased cortical excitability during motor imagery after disuse of an upper limb in humans. Clin.Neurophysiol. 2003;114(12):2397-403.
[67] Kasai T, Kawai S, Kawanishi M, Yahagi S. Evidence for facilitation of motor evoked potentials (MEPs) induced by motor imagery. Brain Res. 1997;744(1):147-50.
[68] Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MV. Studies of illness in the age. The Index of ADL. A standardised measure of biological and psychosocial function. J Am Med SS 1963;185:914-9.
[69] Kim GS. The development of a six component force/moment testing machine and evaluation of its uncertainty. Meas Sci Technol 2000;11:1377-82.
[70] Kitada R, Naito E, Matsumura M. Perceptual changes in illusory wrist flexion angles resulting from motor imagery of the same wrist movements. Neuroscience 2002;109(4):701-7.
[71] Knott M, Voss D. Facilitation neuromusculaire proprioceptive. Schémas et techniques de kabat. Paris: 1977.
[72] Koo TK, Mak AF, Hung L, Dewald JP. Joint position dependence of weakness during maximum isometric voluntary contractions in subjects with hemiparesis. Arch.Phys.Med.Rehabil. 2003;84(9):1380-6.
[73] Kuhtz-Buschbeck JP, Mahnkopf C, Holzknecht C, Siebner H, Ulmer S, Jansen O. Effector-independent representations of simple and complex imagined finger movements: a combined fMRI and TMS study. Eur.J.Neurosci. 2003;18(12):3375-87.
[74] Lafleur MF, Jackson PL, Malouin F, Richards CL, Evans AC, Doyon J. Motor learning produces parallel dynamic functional changes during the execution and imagination of sequential foot movements. Neuroimage. 2002;16(1):142-57.
[75] Le Bozec S, Goutal S, Bouisset S. Dynamic postural adjustments associated with the development of isometric forces in sitting subjects. Life Sciences 1997;320:715-20.
[76] Lee. Mining in a Data-flow Environment: Experience in Network Intrusion Detection. San Diego: 1999.
[77] Li CR. Impairment of motor imagery in putamen lesions in humans. Neurosci.Lett. 2000;287(1):13-6.
[78] Lorenzo J, Ives JC, Sforzo GA. Knowledge and imagery of contractile mechanisms do not improve muscle strength. Percept.Mot.Skills 2003;97(1):141-6.
[79] Luft AR, Skalej M, Stefanou A, Klose U, Voigt K. Comparing motion- and imagery-related activation in the human cerebellum: a functional MRI study. Hum.Brain Mapp. 1998;6(2):105-13.
[80] Lutz RS. Covert muscle excitation is outflow from the central generation of motor imagery. Behav.Brain Res. 2003;140(1-2):149-63.
[81] Malouin F, Richards CL, Jackson PL, Dumas F, Doyon J. Brain activations during motor imagery of locomotor-related tasks: a PET study. Hum.Brain Mapp. 2003;19(1):47-62.
[82] Mannila, Toivonen. Discovering Frequent Episodes in Sequences. Montreal: 1995.
[83] Mathiowetz V, Kashman G, Volland G, Weber K, Dowe M, Rogers S. Grip and pinch strength: Normative data for adults. Arch.Phys.Med.Rehabil. 1985;66:69-74.

[84] Michalski, Stepp. Automated Construction of Classifications Conceptual Clustering versus Numerical Taxonomy. IEEE Trans on pattern analysis and machine learning 1983;5.
[85] Millar BD. A new metric for data clustering: Bayesian Clustering by Dynamics. Joint Statistical Meetings. Toronto: 1994.
[86] Morganti F, Gaggioli A, Castelnuovo G, Bulla D, Vettorello M, Riva G. The use of technology-supported mental imagery in neurological rehabilitation: a research protocol 11. Cyberpsychol.Behav. 2003;6(4):421-7.
[87] Mulder T, Zijlstra S, Zijlstra W, Hochstenbach J. The role of motor imagery in learning a totally novel movement. Exp.Brain Res. 2004;154(2):211-7.
[88] Muller-Gethmann H, Rinkenauer G, Stahl J, Ulrich R. Preparation of response force and movement direction: onset effects on the lateralized readiness potential. Psychophysiology 2000;37(4):507-14.
[89] Nair DG, Purcott KL, Fuchs A, Steinberg F, Kelso JA. Cortical and cerebellar activity of the human brain during imagined and executed unimanual and bimanual action sequences: a functional MRI study. Brain Res.Cogn Brain Res. 2003;15(3):250-60.
[90] Naito E, Kochiyama T, Kitada R, Nakamura S, Matsumura M, Yonekura Y et al. Internally simulated movement sensations during motor imagery activate cortical motor areas and the cerebellum. J.Neurosci. 2002;22(9):3683-91.
[91] Naito E, Sadato N. Internal simulation of expected sensory experiences before movements get started. Rev.Neurosci. 2003;14(4):387-99.
[92] Page SJ, Levine P, Sisto SA, Johnston MV. Mental practice combined with physical practice for upper-limb motor deficit in subacute stroke. Phys.Ther. 2001;81(8):1455-62.
[93] Page SJ, Levine P, Sisto S, Johnston MV. A randomized efficacy and feasibility study of imagery in acute stroke. Clin.Rehabil. 2001;15(3):233-40.
[94] Papaxanthis C, Pozzo T, Skoura X, Schieppati M. Does order and timing in performance of imagined and actual movements affect the motor imagery process? The duration of walking and writing task. Behav.Brain Res. 2002;134(1-2):209-15.
[95] Papaxanthis C, Schieppati M, Gentili R, Pozzo T. Imagined and actual arm movements have similar durations when performed under different conditions of direction and mass 35. Exp.Brain Res. 2002;143(4):447-52.
[96] Peebles L, Norris BJ. ADULTDATA, The handbook of adult anthropometric and strenght measurements - Data for design safety.Department of Trade and Industry, London, UK 1998.
[97] Perfetti C. Der hemiplegische Patient. Kognitiv-therapeutische Ubungen. München: Richard Pflaum Verlag GmbH & Co; 1997.
[98] Pfurtscheller G, Neuper C. Motor imagery activates primary sensorimotor area in humans. Neurosci.Lett. 1997;239(2-3):65-8.
[99] Pfurtscheller G, Neuper C, Ramoser H, Muller-Gerking J. Visually guided motor imagery activates sensorimotor areas in humans. Neurosci.Lett. 1999;269(3):153-6.
[100] Pfurtscheller G. Spatiotemporal ERD/ERS patterns during voluntary movement and motor imagery. Suppl Clin.Neurophysiol. 2000;53:196-8.
[101] Popivanov D, Likova L, Sauleva Z. EEG frequency dynamics during movements imagery. Acta Physiol Pharmacol.Bulg. 2001;26(1-2):115-8.
[102] Porro CA, Francescato MP, Cettolo V, Diamond ME, Baraldi P, Zuiani C et al. Primary motor and sensory cortex activation during motor performance and motor imagery: a functional magnetic resonance imaging study. J.Neurosci. 1996;16(23):7688-98.
[103] Porro CA, Cettolo V, Francescato MP, Baraldi P. Ipsilateral involvement of primary motor cortex during motor imagery. Eur.J.Neurosci. 2000;12(8):3059-63.

[104] Ramoni M, Sebastiani P, Cohen P. Bayesian Clustering by Dynamics. Machine Learning 2002;74(1):91-121.
[105] Reinkensmeyer DJ, Dewald JP, Rymer WZ. Guidance-based quantification of arm impairment following brain injury: a pilot study. IEEE Trans.Rehabil.Eng 1999;7(1):1-11.
[106] Ridgeway G. Finite discrete Markov process clustering. Microsoft Research.Advanced Technical Division, Technical Report 1997;MSR-TR 97(24).
[107] Rossini PM, Rossi S, Pasqualetti P, Tecchio F. Corticospinal excitability modulation to hand muscles during movement imagery. Cereb.Cortex 1999;9(2):161-7.
[108] Schmit BD, Dewald JP, Rymer WZ. Stretch reflex adaptation in elbow flexors during repeated passive movements in unilateral brain-injured patients. Arch.Phys.Med.Rehabil. 2000;81(3):269-78.
[109] Schwoebel J, Boronat CB, Branch CH. The man who executed "imagined" movements: evidence for dissociable components of the body schema. Brain Cogn 2002;50(1):1-16.
[110] Sergio LE, Kalaska JF. Systematic changes in directional tuning of motor cortex cell activity with hand location in the workspace during generation of static isometric forces in constant spatial directions. J.Neurophysiol. 1997;78(2):1170-4.
[111] Sergio LE, Kalaska JF. Changes in the temporal pattern of primary motor cortex activity in a directional isometric force versus limb movement task. J.Neurophysiol. 1998;80(3):1577-83.
[112] Sergio LE, Kalaska JF. Systematic changes in motor cortex cell activity with arm posture during directional isometric force generation. J.Neurophysiol. 2003;89(1):212-28.
[113] Sirigu A, Duhamel JR. Motor and visual imagery as two complementary but neurally dissociable mental processes. J.Cogn Neurosci. 2001;13(7):910-9.
[114] Sparing R, Mottaghy FM, Ganis G, Thompson WL, Topper R, Kosslyn SM et al. Visual cortex excitability increases during visual mental imagery--a TMS study in healthy human subjects. Brain Res. 2002;938(1-2):92-7.
[115] Stevens JA, Stoykov ME. Using motor imagery in the rehabilitation of hemiparesis 13. Arch.Phys.Med.Rehabil. 2003;84(7):1090-2.
[116] Stinear CM, Byblow WD. Motor imagery of phasic thumb abduction temporally and spatially modulates corticospinal excitability. Clin.Neurophysiol. 2003;114(5):909-14.
[117] Theeuwen M, Gielen CC, Miller LE. The relative activation of muscles during isometric contractions and low-velocity movements against a load. Exp.Brain Res. 1994;101(3):493-505.
[118] Thomas L. The youngest science. Penguin Booksed. Alfred P.Sloan Foundation Program; 1995.
[119] Toivonen. Discovery of Frequent Patterns in Large Data Collections [dissertation]. University of Helsinki, Department of Computer Science; 1996.
[120] Tomasino B, Rumiati RI, Umilta CA. Selective deficit of motor imagery as tapped by a left-right decision of visually presented hands. Brain Cogn 2003;53(2):376-80.
[121] Tremblay F, Tremblay LE, Colcer DE. Modulation of corticospinal excitability during imagined knee movements. J.Rehabil.Med. 2001;33(5):230-4.
[122] Trochim, W. (2000). The Research Methods Knowledge Base, 2nd Edition. Atomic Dog Publishing, Cincinnati, OH
[123] van Bolhuis BM, Medendorp WP, Gielen CC. Motor unit firing behavior in human arm flexor muscles during sinusoidal isometric contractions and movements. Exp.Brain Res. 1997;117(1):120-30.

[124] van Zuylen EJ, Gielen CC, Denier van der Gon JJ. Coordination and inhomogeneous activation of human arm muscles during isometric torques. J.Neurophysiol. 1988;60(5):1523-48.
[125] Walsh SM, Saltzman CL, Talbot KD, Aper RL, Brown TD. In vivo validation of in vitro testing of hallucal flexor mechanics. Clin Biomechanics 1996;11:328-2.
[126] Warner L, McNeill ME. Mental imagery and its potential for physical therapy. Phys.Ther. 1988;68(4):516-21.
[127] Weiss, Indurkhya. Predictive Data Mining. A practical Guide. Morgan Kaufmann Publishers; 1998.
[128] Wilson PH, Thomas PR, Maruff P. Motor imagery training ameliorates motor clumsiness in children. J.Child Neurol. 2002;17(7):491-8.
[129] Woldag H, Hummelsheim H. Evidence-based physiotherapeutic concepts for improving arm and hand function in stroke patients: a review. J.Neurol. 2002;249(5):518-28.
[130] Yaguez L, Nagel D, Hoffman H, Canavan AG, Wist E, Homberg V. A mental route to motor learning: improving trajectorial kinematics through imagery training. Behav.Brain Res. 1998;90(1):95-106.
[131] Yahagi S, Shimura K, Kasai T. An increase in cortical excitability with no change in spinal excitability during motor imagery. Percept.Mot.Skills 1996;83(1):288-90.
[132] Young MS, Triggs WJ, Pendergast JF, Heilman KM. The effects of selective response preparation on corticospinal excitability. Cortex 2000;36(1):19-29.
[133] Zijdewind I, Toering ST, Bessem B, Van Der LO, Diercks RL. Effects of imagery motor training on torque production of ankle plantar flexor muscles. Muscle Nerve 2003;28(2):168-73.