This is a repository copy of *Case Study of Patients Participating in a Randomised Controlled Trial of Upper-Limb Robotic Rehabilitation in Acute Stroke Services*.

Case study of patients participating in a randomised controlled trial of upper-limb robotic rehabilitation in acute stroke services.

A.E. Jackson, M.C. Levesley
School of Mechanical Engineering
University of Leeds
Leeds, UK

J.A. Cozens
Department of Rehabilitation Medicine
Grampian NHS
Aberdeen, UK

S.G. Makower
Leeds Community Healthcare NHS Trust
Leeds, UK

R. J. O'Connor
Faculty of Medicine and Health
University of Leeds and
Leeds Teaching Hospitals Trust, UK

Abstract— **This paper presents some findings from a randomised controlled trial in patients with upper-limb weakness in acute stroke services within the UK's National Health Service. Three patients were selected from the robot arm of the trial; one who exhibited a large increase in Fugl-Meyer score (change > 30); one who exhibited a moderate change (10 < change < 20) and a subject who demonstrated no change between baseline and follow-up. The results from robot assistance level and target achievement over the course of the treatment are presented for the three patients, demonstrating the system's ability to automatically alter the assistance level as patients progress.**

Keywords- robotic rehabilitation, stroke, upper limb, randomised control trial.

I. INTRODUCTION

Stroke is the leading cause of adult disability in the UK, every year 152,000 people have a stroke. Of those who survive, approximately half experience physical disability with upper-limb weakness being the most common impairment. Upon discharge from hospital, around 37% of survivors will require assistance with activities of daily living (ADL) [1]. The average cost per patient of care and rehabilitation is £23,315 (34,750 USD) leading to a total Health and social care costs bill of approximately £4.38bn (6.53bn USD). This places a significant financial and resource burden on the NHS leading to overstretched stroke services. It is recognised that the most recovery occurs in the first few weeks following stroke, this is seen as a result of the combination of rehabilitation and spontaneous recovery, however due to limited therapy resources patients spend the majority of their time during this acute stage in their beds. This may lead to sub-optimal recovery as it is recognised that recovery is related to the frequency and quality of therapeutic intervention [2,3].

By utilising assistive robotic systems to supplement conventional rehabilitation, it is possible to increase the intensity of therapeutic exercises patients receive without a significant increase in therapy resources. This is especially desirable in the acute stages of stroke, while patients are still within the hospital environment. Robotic systems are designed to undertake some of the repetitive movement tasks required for functional recovery of the arm, freeing up therapists to undertake more complex targeted intervention for which robotic systems may be unsuitable. The overall aim being that patients can spend more time engaged in therapeutic exercise than with conventional therapy alone.

Rehabilitation robotics is a large and growing area of research with an ever expanding number of systems being developed internationally. As these systems are developed and in some cases commercialised, there is a growing body of evidence as to the efficacy of providing therapeutic exercise to the upper-limb via a robotic system. A review of upper-limb robotic stroke rehabilitation [4] cited 28 such robotic systems. These systems are configured in one of two ways; either as an end-effector based robotic arm whereby the patient interacts with the patient via a handle or wrist orthosis; or an exoskeleton system that has several contact points along the arm with robot joints coincidental with the human joints. An example of the former type is the MIT-Manus [5]. Probably the most established and clinically proven upper-limb rehabilitation system, it has been commercialised as the InMotion ARM™ Interactive Therapy System. It is a planar two DoF robotic arm system which can include additional attachments for the hand to increase functionality. A second end-effector based system is the Arm-Guide [6] works on an adaptable linear slide mechanism. Both systems have been assessed in randomised controlled trials.

An example of an exoskeleton system is ARMin. ARMin [7] is a seven DoF exoskeleton robot system that provides task-specific exercise to people with stroke. Allowing three dimensional exercise, the system provides relatively large workspace, also incorporating a hand opening and closing mechanism.

The aforementioned systems all feature in a Cochrane review of randomised controlled trials (RCTs) for upper-limb robotic stroke rehabilitation [8]. It looked at the outcomes of 19 trials involving 666 participants. Primary outcomes were concerned with Activities of Daily Living with secondary outcomes looking at motor function (Fugl-Meyer Assessment – Upper Extremity) and muscle strength. Conclusions of the review stated that robotic systems for upper-limb rehabilitation are more effective that other interventions when considering ADLs and motor function, however the authors state that the changes are such that they may have a limited effect on the clinical meaning for the patient.

A more recently published RCT [9] using the ARMin system recruited 77 patients who were at least six months post-stroke and delivered a total of 24 sessions of robot or conventional therapy depending on the trial arm. Their findings showed a minor difference between conventional and robotic therapy, inferring that robotic therapy could be more beneficial that conventional therapist delivered therapy however improvements in Fugl-Meyer Upper Extremity Assessment were still small for each group; 3.25points (SD1.68) for robotic therapy and 2.47 points (SD1.67) for control arm. As highlighted above, the effects of this improvement on patient's clinical outcome may be limited.

iPAM (intelligent Pneumatic Arm Movement) is a robotic system developed at the University of Leeds to provide assistive upper-limb exercise to a wide range of patients with arm weakness as a result of stroke. It combines the mechanical simplicity and ease of attachment of an end-effector system with the human-joint control benefits of an exoskeleton system while proving a large workspace. This paper presents some results from a RCT undertaken with three iPAM MkII systems within acute stroke services in the UK National Health Service. The iPAM MkII system is introduced followed by a description of the RCT and summary of the experience. There then follows a small case study relating assistance level provided by the robots and the exercise target achievement when looking at three patients with differing outcomes.

II. iPAM MkII

Developed by a multidisciplinary team including engineers, rehabilitation physicians, therapists, stroke survivors and their carers, iPAM has been specifically designed to meet the needs of the various stakeholders, helping to ensure end-user acceptance. The design process for both the iPAM MkI and MkII can be found in [10] and [11] respectively.

A. Hardware

Mimicking the method in which a therapist provided assistive exercise to the human arm, the robot consists of two identical robot arms attached to a base unit. Each arm has three pneumatically-actuated revolute joints, allowing control of the robot end-points in Cartesian space. At the end of each robot arm are detachable orthoses (easily swappable for left and right sided operation) that allow three

passive rotational DoF aligned with the centre of the human arm to ensure the arm is always comfortably aligned within the system. A distal orthosis attaches to the lower arm close to the wrist while the proximal orthosis attaches to the upper-arm around the mid-point between the elbow and shoulder. As the arm is calibrated within the system at the start of each session, the exact positioning of the orthoses on the arm is not required, making attaching the robot a quick process.

Each end-effector contains a JR3 six DoF force/torque transducers for measuring the robot/patient interaction force while each robot joint contains a rotary sensor for measuring joint position. An air pressure sensor and patient and emergency stop buttons are used to ensure safe operation of the system.

Low-level control is undertaken on a dedicated embedded controller running deterministic real-time software while a standard personal computer provides communication protocols and runs the high-level supervisory control and the patient and clinician interfaces (SILCK clinic).

Additional hardware consists of a standard wheelchair with a modified back rest that allows a large range of movement close to the body; a docking station that holds the calibration tools and locates the wheelchair correctly relative to the robot base unit; a large LCD display that presents the patient interface to the user allowing the patient to engage with the system; and a stand-alone low-noise medical grade air-compressor. The iPAM MkII system can be seen in Figure 1.

Figure 1. The iPAM MkII Robotic Rehabilitation System

B. Control

As the two robots are independent it is essential that they coordinate effectively; any misalignment of the end effectors could result in excessive torques being applied to the patient's limb. As such a control strategy was developed that controls the robots using a six DoF model of the human arm. With three active DoF at each robot end-effector it is possible to control six DoF of the human arm, two translational and three rotational DoF at the shoulder, and a single rotational DoF at the elbow. By providing control through the human arm model in human task space rather than the robot task space it is possible to ensure safe

coordination of the two robotic arms. Trajectories are passed from the high-level controller in the form of human joint positions and rotations, target locations and admittance control parameters. When exercises commence the robot enters a parked position moving the patients arm to a comfortable location close to the patients lap. The patient is then presented with a virtual target to which they should reach towards; iPAM will assist them to reach the target.

The system utilises an admittance control scheme to modulate the demand position of the robots based on the measured human joint torques and forces. The admittance function modulates the input trajectory for each human DoF as a function of measured force/torque and takes the form:

$$\delta x = F /(Kx + Cx.s) \quad (1)$$

where K and C are stiffness and damping terms respectively. An exponential mapping function is used for converting the assistance level in terms of percentage as seen by the physiotherapist to the stiffness term K used by the admittance controller. For rotary joints, 100% sets a joint stiffness of 40Nm/rad while 0% gives 0.075Nm/rad. Damping is static at 0.25Nms/rad. Translational DoF at shoulder maintained a high stiffness setting throughout. The new demand positions for the human joints are then converted to robot end-effector positions using the forward kinematics of the human arm. The inverse kinematics of the robot arms are then used to calculate the desired robot joint angles. PID controllers are used at each robot joint to provide the position control. A detailed description of the control system has been presented previously [12].

C. Operation

A typical iPAM treatment session will last for 1 hour and consist of approximately 40 to 45mins of robot-assisted exercise although this will vary from patient to patient. At the beginning of a treatment session, the system initialises into a passive operating mode called warm standby. In this mode the robots are supporting their own weight such that they are free to move around. This is an inherent benefit of using pneumatic actuators, the pressure regulating valves are set to maintain a specific pressure, manually moving the robots causes the pressure on one side of the low friction pneumatic cylinders to increase while decreasing it on the other, the pressure regulating valves quickly adapt to reduce the higher pressure and increase the lower pressure balancing the pressure. This makes the whole system innately back-driveable.

Patients are seated in the chair and their trunk secured using a four point harness. This is to prevent excessive trunk movement, ensuring the movement is predominantly as a result of arm use. A shoulder monitor consisting of three pull-cord potentiometers is attached to the shoulder using medical tape. This provides the relative movement of the shoulder to an initialised position which is fed into the inverse kinematics solver for the human arm model, improving accuracy. It is also used as a safety check to detect a change in patient posture. The orthoses are then attached. They use a modified blood pressure cuff that can gently hold the arm in place while a barrier material with a

high-friction coating is used to ensure the orthosis does not slip during use.

The next stage is to calibrate the patient's arm within the system. This is to match the human arm model used by the controller with the patient's arm. Two custom tools are used to take measurements, one giving the relative positon of the orthoses to bony markers on the limb and the second providing the initial shoulder offset from the robot base unit. Once calibrated the attending therapist or assistant undertakes a visual inspection of the calibrated arm model, matching the 3D representation of the arm shown on the patient interface and the real arm.

Once calibrated the therapist must prescribe an exercise set for the patient to undertake. These are set through the high-level clinician interface (SILCK clinic). This provides the therapist with the mechanism for converting clinical assessment of the patient into robot specific information used to develop exercise prescriptions. Exercises sets can consist of fixed tasks or open tasks:

Fixed tasks: These involve the physical recording of a specific arm movement trajectory by guiding the patient's arm through a specific movement while the robot records the trajectory in terms of human joint angles, this can then be replayed by the system as an exercise. A push button on the proximal robot handle is used to set virtual target locations.

Open tasks: These involve the selection of a specific treatment strategy that is suitable for the particular patient. Depending on strategy chosen, the system will automatically generate movement trajectories tailored to the particular treatment strategy. Open tasks consist of exercises featuring movements between 8 separate targets. Targets appear on the patient interface along with the 3D representation of the patient's limb (Fig. 2).
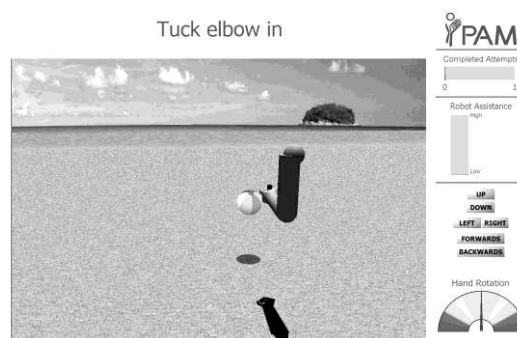

Figure 2. Patient Interface screen appear on a large display infront of patient during exercise and displays human arm model and virtual targets.

The two categories of open task exercises are:

Category A: This strategy is suitable for patients with limited arm movement or high-tone at the elbow and/or shoulder, the strategy aims to gradually increase the range of movement by undertaking small reach/retrieve movements at either table level or at an increasing elevation. The controller will automatically increase the range of movement as the patient successfully and consistently

reaches the target locations. The strategy will also introduce lateral movements as the patient progresses. The assistance level (K value in admittance controller) is set manually by the therapist.

Category B: This strategy is suitable for those with a wide range of movement deficits but is not suitable for patients with high tone. This strategy commences with a number of simple, limited range reach/retrieve exercises to warm-up the patient. The workspace is then separated up into four outer-reach quadrants and the system will undertake a number of movements exploring each quadrant in turn. All targets are placed within a safe workspace for the patient, physically defined by the therapist. As patients consistently reach targets over consecutive exercise attempts, the assistance level will drop at 5% intervals. The therapist has the choice to remove specific quadrants from the prescription and to manually intervene in the assistance setting.

Once the appropriate exercise prescription has been chosen the therapist can select the desired number of exercise attempts and the duration of the exercise session. The exercise set can then commence with the patient only requiring indirect therapist or assistant supervision. The patient has a patient stop button on their unaffected side to halt the exercise set at any time; alerting the therapist via an audible and visual alarm. At the end of the session, the system returns to warm standby and the orthoses are quickly removed allowing the patient to exit the system.

III. RANDOMISED CONTROL TRIAL

The iPAM MkII system has successfully been used as part of an RCT within acute stroke services of the NHS. Initially iPAMs were installed in three different NHS trusts hospitals in Hull, Pontefract and Aberdeen. The aims of the RCT were to determine the feasability and practicalities of delivering a RCT using iPAM within NHS stroke services; to obtain clinical outcome data to determine appropriate sample sizes for future Phase 3 clinical trial design and to assess the safety of the system within a clinical environment.

A. Trial design

A prospective, randomised, controlled trial of NHS rehabilitation treatment alone verses NHS rehabilitation treatment with up to 6 weeks iPAM treatment (up to 30 sessions) for patients admitted to acute stroke services after a new stroke. It was proposed that 90 patients with acute stroke were recruited across three NHS stroke units. Exlcusion criteria were based on the patient's medical stability, having no pre-stroke arm movement deficit and weight (max 125kg limited by wheelchair).

In total, 51 patients were recruited to the trial. Twenty-six patients were recruited to the active group and twenty-five to the control group. Unfortunately shortly after installation of the third iPAM system at Pontefract General Infirmary, stroke services within the NHS trust were restructured and early supported discharge introduced. This had an effect on recruitment for the trial. After 6 months, only three patients had been recruited for the site, one for

the robot arm and two for the control arm. At this stage it was decided that the Pontefract site should be removed from the trial.

Additional issues occurred at Hull Royal Infirmary when an outbreak of gastroenteritis resulted in the ward closing. During this time a patient recruited to the robot arm of the trial was unable to receive any treatment. The therapy gym in Aberdeen was also closed for an extended period during the trial period due to renovation work; this led to the system remaining unused for around four months during the two-year trial.

B. Intervention

1) Active group: each patient recruited to the iPAM group received one to two exercise sessions of iPAM delivered therapy per day for up to 30 days on top of usual therapy. Each exercise session was approximately 45-60 minutes or, on occaision, as low as 10 minutes depending on the patient's clinical state. iPAM intervention with usual NHS rehabilitation treatments was continued for a maximum of six weeks. The duration of treatment was less if the patient: completes 30 iPAM exercise sessions; no longer requires therapy; is discharged from hospital (patients were offered the opportunity to come back to hospital to complete their course of trial therapy); or there is lack of stroke unit staff time to deliver the intervention. The decision about need for rehabilitation interventions was made by the treating clinicians, therapists and nurses in consultation with patients and families as part of the routine management of the patient.

2) Control group: The control group received usual therapy plus additional matched therapy time. It was estimated from previous patient experience that it takes a maximum of 15 minutes to set up the iPAM system and prescribe iPAM exercises for each treatment session. Therefore on a weekly basis, a maximum of 2.5 hours (maximum of two 15 minutes sessions, 5 times per week) extra therapy treatment per week was allocated to the control group. To be efficient, this extra time therapy was often combined or added to usual therapy intervenstion to make extra or longer usual therapy sessions. This provided a matched burden on therapy resource between the active and control group.

C. Outcomes

The primary outcome for the RCT was a clinically meaningful response (defined as >=3 point improvement in Fugl Meyer (Upper limb section) score [13]) from baseline to 10 weeks post randomization. Secondary outcome measures were: Barthel Index; Stroke Impact Scale; ABILHAND; EQ-5D. Results of the clinical outcome measures are not included in this paper

D. Trial discussion

Over the course of the trial, the iPAM systems undertook over 12,500 exercise tasks with no adverse events recorded. The Aberdeen system was in use for 1 year, 11 months and 28 days from the first patient session to the last (including the 4 months during which the system went into storage), while the Hull system was in use for 1 year, 7 months and 6

days. While several minor technical issues occurred that required a member of the project team to visit the site, the safety systems and protocols incorporated into the system ensured that none of these resulted in patient harm. As a result it was clearly demonstrated that the system could operate safely in a clinical environment by suitably trained therapy staff. The overall change in Fugl-Meyer Assessment – Upper Extremity score across both cohorts was +16.3 (15.3SD).

IV. CASE STUDY RESULTS

During a standard exercise attempt the iPAM system records a wealth of data that is stored for later analysis. There are several key parameters that can be used to analyse the interaction between the robot and patient. A key feature of the system as described above is its ability to automatically adjust assistance settings based on patient achievement. This paper will look at three particular patients who exhibited different clinical outcomes and compare these outcomes with some parameters measured by the robot system. The patient details are presented in Table 1. It should be noted that patients during the trial received a varied level of both robot and conventional therapist upper-limb intervention, with Patient A receiving approximately double the intervention as Patient C.

The patients chosen predominantly used the Category B type exercise prescriptions such that as the patient improved, achieving more targets during the exercises they would see iPAM automatically reducing the assistance level in 5% increments. Each time the assistance level drops, the patient must contribute more to the exercise to achieve the same number of targets (maximum of eight per exercise attempt). In all patients using this strategy we would expect to see some early drop off of the assistance level. This is because at 100% assistance the system will have very high admittance parameters, leading to the system behaving in position control. In this case iPAM is capable of moving the arm to the targets without patient effort. It should be the case that after this initial reduction of assistance setting, any changes to assistance level would be a result of an improvement in patient movement. In a recovering patient we would expect to see the assistance level consistently dropping over time while the target achievement would drop slightly at each reduction of assistance before increasing again to an attainment close to 8 targets per exercise. It would be envisioned that this continual improvement would continue while the patient improved and that by the time assistance was down to less than 20%, the patient would require very little robot assistance and as such may no longer need iPAM. A target is achieved when the hand reaches to within 5cm of the virtual target position while a near-miss is set to a 7.5cm radius. For this treatment strategy, should a patient consistently hit far targets over course of five consecutive exercises, the assistance will be lowered by 5%.

Fig. 3 shows the assistance level for the three patients over the course of the treatment sessions. Patient A demonstrates a continued improvement as the session progress, reducing down to 45% by the end of the treatment. Note that assistance often increases to a higher value after an initial reduction. SILCK clinic will increase assistance should a patient be unable to consistently achieve a near miss on far reach targets over 5 consecutive exercises. In the case of Patients B and C, it can be seen that there is little reduction in assistance overall however it can be seen in this case, Patient C actually achieves a lower assistance level than patient B, despite a higher FM score at both baseline and follow-up.

Figs. 4, 5 and 6 show the assistance level and target achievement against exercise attempt for the three patients, A, B and C respectively. To reduce the noise in the target achievement data, the line shown is the average value of each 10 exercise attempts. A value of 8 would mean every target over 10 consecutive exercise attempts was achieved. In the case of Patient A (Fig. 4), while assistance level drops over the course of the treatment, the rate of target achievement stays between 5.8 and 8. This signifies that even though the assistance given by the robot is decreasing over the course of the treatment, the patient is maintains the ability to reach the targets, clearly demonstrating an improvement in patient ability as the change in FM score would suggest. It can be seen from Fig. 5 that patient B has a long period where they are unable to get consistent target achievement and during this period no change in assistance setting occurs. This last approximately 600 exercises at which point the patient begins to achieve a higher level of target achievement leading to a reduction in assistance which is then temporarily reversed at around 1000 exercises before again returning to a lower assistance. It is unclear from the clinical notes whether there was any change at the patient that led to the change at 800 exercises in. Patient C (Fig. 6) demonstrates a slow decrease in assistance over the treatment.
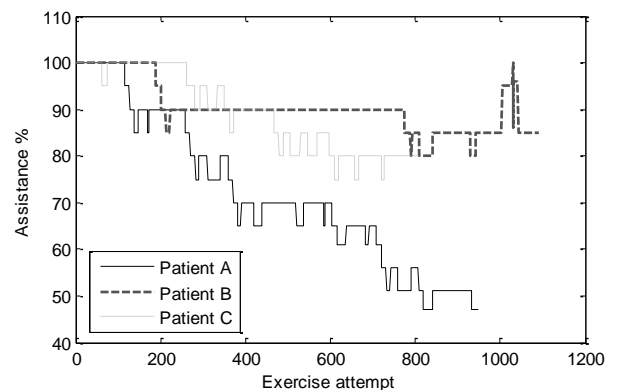

Figure 3.   Assistance level vs exercise attempt for Patients A, B and C.

TABLE I.   PATIENT INFORMATION

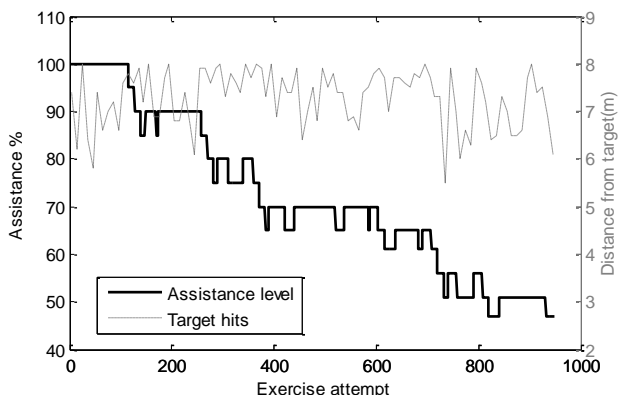| Patient	Sex	Trial Site	Affected Side	Age at sign-up	Type of stroke	Baseline Fugl Meyer /66	Follow-up Fugl Meyer /66	Change in Fugl Meyer	Standard therapy (min)	Robotic therapy (min)
A	Male	Hull	Right	38	Infarction	10	48	38	1245	1026
B	Male	Aberdeen	Left	66	Infarction	23	38	15	620	1079
C	Male	Aberdeen	Right	48	Infarction	4	4	0	340	741

Figure 4.   Assistance level and target achievement for Patient A.
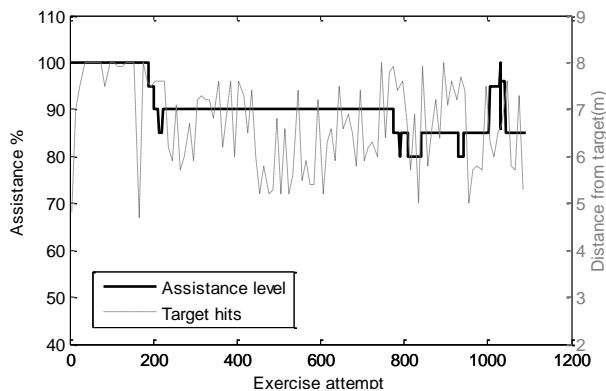

Figure 5.   Assistance level and target achievement for Patient B.
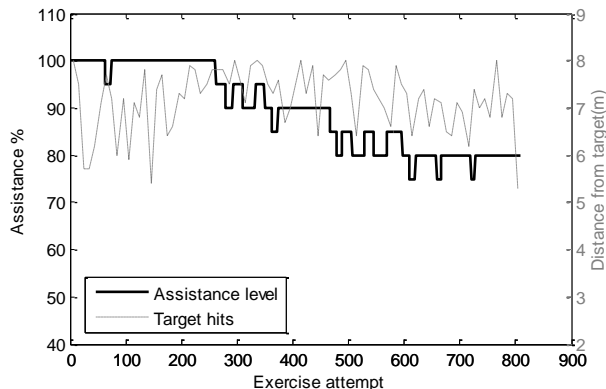

Figure 6.   Assistance level and target achievement for Patient C.

V.   CONCLUSION

This paper presents the iPAM MkII robot system and the rationale of a randomised control trial it was used in. A case study of three patients was presented demonstrating the system's ability to detect improvements in patient performance and adjust assistance level accordingly. A link between Fugl-Meyer score and robot assistance levels with three patients is discussed each demonstrating a different outcome from the trial. This provides therapists with a means of undertaking frequent quantitative assessment of patient performance and improvement as the treatment progresses; a task that is impractical using standard clinical measures.

REFERENCES

[1]   Stoke Association "State of the nation – Stroke statistics – January 2015" http://www.stroke.org.uk. Accessed January 2015.

[2]   G. Kwakkel, R. C. Wagenaar, J. W. R. Twisk G. J. Lankhorst, J. C. Koetsier, "Intensity of leg and arm training after primary middle cerebral artery stroke: a randomized trial." Lancet 1999;354:189-194.

[3]   A. Sunderland, D. J. Tinson, E. L. Bradley, D. Fletcher, R. Langton Hewer, D. T. Wade, "Enhanced physical therapy improves recovery of arm function after stroke. A randomized controlled trial." J Neurol Neurosurg Psychiatry 1992;55(7):530-535.

[4]   R. C. V. Loureiro, W. S. Harwin, K. Nagai, M. Johnson, "Advances in upper-limb stroke rehabilitation: a technology push". Medical & Biological Engineering & Computing, Oct 2011, 49(10), pp 1103-1118

[5]   H. I. Krebs , M. Ferraro, S. P. Buerger, M. J. Newbery, A. Makiyama, M. Sandmann, D. Lynch, B. T. Volpe, N. Hogan, "Robotic upper-limb neurorehabilitation in chronic stroke patients". Journal of Neuro Engineering and Rehabilitation, 1:5 2004.

[6]   D. J. Reinkensmeyer, C. D. Takahashi, W. K. Timozyk, A. N. Reinkensmeyer, L. E. Khan, "Design of robot assistance for arm movement therapy following stroke." Advanced Robotics, Vol. 47(7), pp. 625-637, 2001.

[7]   T. Nef, M. Guidali, V. Klamroth-Marganska, R. Riener, "ARMin – Exoskeleton Robot for Stroke Rehabilitation." Proceedings of World Congress on Medical Physics and Biomedical Engineering, 2009. pp. 127-130.

[8]   J. Mehrholz, A. Hädrich, T. Platz,J. Kugler, M. Pohl, "Electromechanical and robot-assisted arm training for improving generic activities of daily living, arm function, and arm muscle strength after stroke.", Cochrane Database Syst Rev, 2012 Jun 13;6.

[9]   V. Klamroth-Marganska. J. Blanco, K. Campen, A. Curt, V. Dietz, T. Ettlin, M. Felder, B. Fellinghauer, M. Guidali, A. Kollmar, A. Luft, T. Nef, C. Schuster-Amft, W. Stahel, R. Riener, "Three-dimensional, task-specific robot therapy of the arm after stroke: a multicentre, parallel-group randomised trial". The Lancet Neurology. Volume 13, Issue 2 pp. 159-166. 2014.

[10]   A. E. Jackson, R. J. Holt, P. R. Culmer, S. G. Makower, M. C. Levesley, R. C. Richardson, J. A. Cozens, M. Mon-Williams, B. B. Bhakta, "Dual Robot System for Upper Limb Rehabilitation after Stroke: The Design Process." Proceedings of the IMechE. Part C - Journal of Mechanical Engineering Science. Volume 221, No. 7, 2007, pp. 845-857.

[11]   A. E. Jackson, S. G. Makower, M. C. Levesley, J. A. Cozens, B. B. Bhakta, "Development of the iPAM MkII system and description of a randomized control trial with acute stroke patients." Proceedings of the International Conference on Rehabilitation Robotics 2013.

[12]   P. R. Culmer, A. E. Jackson, J. Savage, M. C. Levesley, R. Richardson, J. A. Cozens, B. B. Bhakta, "An Admittance Control Scheme for a Robotic Upper-Limb Stroke Rehabilitation System." Proceedings of the 27th Annual Conference IEEE Engineering in Medicine and Biology 2005. pp. 5081-5084.

[13]   A.C. Lo, P. D. Guarino, L. G. Richards, J. K. Haselkorn, G. F. Wittenberg, D. G. Federman et al., "Robot-Assisted Therapy for Long-Term Upper-Limb Impairment after Stroke." N Engl J Med 2010;362, pp. 1772-1783 2010.