A new treatment in the rehabilitation of the paretic upper limb after stroke: the ARAMIS prototype and treatment protocol

Loris Pignolo[1], Lucia F. Lucca[1], Giuseppina Basta[1], Sebastiano Serra[1], Maria E. Pugliese[1], Walter G. Sannita[2] and Giuliano Dolce[1]

[1]*RAN, Ricerca Avanzata in Neuroriabilitazione, Istituto S. Anna, Crotone, Italy*
[2]*Dipartimento di Neuroscienze, Oftalmologia e Genetica, Università degli Studi di Genova, Genoa, Italy*

ORIGINAL ARTICLES AND REVIEWS

Abstract

Background. In recent years, as part of the rehabilitation of post stroke patients, the use of robotic technologies to improve recovery of upper limb has become more widespread. The Automatic Recovery Arm Motility Integrated System (ARAMIS) is a concept robot and prototype designed to promote the functional interaction of the arms in the neurorehabilitation of the paretic upper limb. Two computer-controlled, symmetric and interacting exoskeletons compensate for the inadequate strength and accuracy of the paretic arm and the effect of gravity during rehabilitation. Rehabilitation is possible in 3 different modalities; asynchronous, synchronous and active-assisted.

Objectives. To compare the effectiveness of robotic rehabilitation by an exoskeleton prototype system with traditional rehabilitation in motor and functional recovery of the upper limb after stroke.

Methods. Case-control study, 52 patients enrolled in the study, 28 cases (women: 8, age: 65 ± 10 yrs) treated with ARAMIS and 24 controls (women: 11, age: 69 ± 7 yrs) with conventional rehabilitation.
Motor impairment assessed before and after treatment with Fugl-Meyer scale and Motricity Index, level of disability assessed with the Functional Independence Measure. A questionnaire was also administered to assess the patient's tolerance to robotic therapy.

Results. After 28 ± 4 sessions over a 54 ± 3.6-day period, the patients treated by ARAMIS had an improvement on the Fugl-Meyer scale (global score from 43 ± 18 to 73 ± 29; $p < 0.00001$), Motricity Index scale ($p < 0.004$) and Functional Independence Measure ($p < 0.001$). A lesser degree of improvement was achieved using conventional rehabilitation, the Fugl-Meyer global score of the control group improved from 41 ± 13 to 58 ± 16 ($p < 0.006$) and the motor function item from 9.4 ± 4.1 to 14.9 ± 5.8 ($p < 0.023$).

Conclusions. Motor improvement was greater at the wrist and hand than at shoulder and elbow level in patients treated by ARAMIS and controls, but it was significantly greater in ARAMIS-treated patients than in controls. The results indicate a greater efficacy of ARAMIS compared to conventional rehabilitation.

INTRODUCTION

Stroke is the second most common cause of death and a major cause of disability worldwide [1]. Its rate is increasing due to the increasing age of the population, thus with a resulting increase in motor and cognitive disability and related personal, social and health costs [2, 3]. Interest in the application of robotics in neurorehabilitation is growing [4]. Focus is on the rehabilitation of the paretic upper limb, the recovery of which is often incomplete [5]. Updated Cochrane reviews, however, suggest either improved motor function or muscular strength or daily living activities in the absence of overall significant effects in favor of robot-assisted therapy. Heterogeneities among studies may have reduced the evidence of efficacy, yet the advantages of robot-assisted rehabilitation remain incompletely documented [6, 7].

Address for correspondence: Loris Pignolo, Ricerca Avanzata in Neuroriabilitazione (RAN), Istituto Sant'Anna, Via Siris 11, 88900 Crotone, Italy.
E-mail: l.pignolo@istitutosantanna.it.

The Automatic Recovery Arm Motility Integrated System (ARAMIS) is a concept robot and prototype for the neurorehabilitation of the paretic upper limb after stroke. It has been conceived to take advantage of the functional interaction of the arms and the innervations of the trunk and shoulder that provide anatomical and physiological functional conditions to support potential recovery [8, 9]. To this end, ARAMIS operates two computer-controlled, symmetric and interacting exoskeletons that compensate for the inadequate strength and accuracy of the paretic arm movements and the effect of gravity during rehabilitation. Patient, operator and robot interact. The training exercises and rehabilitation protocols can be personalized in a virtually unlimited variety of modalities and are adjustable during treatment whenever required. ARAMIS can measure the shoulder, elbow and forearm residual motor function in baseline and record quantitative indices of motor recovery during/after treatment [10-14]. The ARAMIS prototype is fully operative at the Institute S. Anna – RAN (Ricerca Avanzata in Neuroriabilitazione) in Crotone, Italy. Applicability, however, depends on acceptability and tolerance as well [15], while the improvement after robot-assisted rehabilitation needs to be at least comparable to traditional rehabilitation. Evidence of a better outcome would support the project rationale and methodological approach while allowing inference about the pathophysiological mechanisms involved in the paretic upper limb motor recovery [15-20]. The purpose of this study was to test the tolerability and efficacy of ARAMIS compared to conventional rehabilitation after stroke.

METHODS
ARAMIS hard/software structure

The robotic platform includes two fully-motorized 6 DOF symmetric exoskeletons *(Figure 1)*. The root joint of each one acts as an interface between the robotic arm and its support in order to reduce the load on the subject [11, 13]. Kinematics and dynamic data at joint level are continuously acquired and stored by the control system that evaluates the weight torque (and compensates for it by controlling each upper limb posture) and the strength delivered by the patient to the exoskeleton; movement is therefore supported by a drive motor adjusting its strength on step by step needs. The system software architecture (the ARAMIS Framework) is a fully integrated set of software that enables the therapist to program and manage the rehabilitation procedures. Each exoskeleton can record (motion capture) the movements of the healthy arm and the patient is requested to replicate each movement by the paretic arm in synchronous or asynchronous modalities depending on the exercise typology or training program, with continuous compensation for the paretic arm's inadequate strength and accuracy. ARAMIS-assisted rehabilitation is possible in three different modalities: 1) asynchronous: the patient wears both exoskeletons and uses the unaffected arm to perform pre-programmed exercises that are replicated by the paretic arm supported by its own exoskeleton; 2) synchronous: the unaffected arm paces the movements to be replicated synchronously and with the same physical characteristics (such as strength, acceleration, range, and speed) by the exoskeleton hosting the paretic arm; 3) active-assisted: when a degree of motor recruitment has been achieved by the patient's paretic arm, the robot supports the arm strength against gravity in movements replicating those executed by the unaffected arm.

Patients and study design

Two groups of patients treated by conventional or robot-assisted (ARAMIS) neurorehabilitation procedures were compared. Sixty patients were recruited among 100 subacute hemiplegic inpatients who had suffered a hemispheric ischemic stroke. Criteria for exclusion were: bilateral impairment; severe sensory deficits in the paretic upper limb; medical implants of any kind, concomitant nonvascular neurological diseases (multiple sclerosis, space occupying lesions, etc.), pregnancy, epilepsy, aphasia, cognitive impairment cognitive impairment (Mini Mental State Evaluation, MMSE < 24) or behavioral dysfunction that would influence the patient's ability to comprehend or participate in the treatment; inability to provide informed consent. Patients who met the inclusion criteria were assigned sequentially to one group then the other *(Figure 2)*. Two patients in robot-assisted and six in conventional therapy discontinued treatment and were excluded from the study because of medical or surgical complications unrelated to the neurological condition and rehabilitation procedures. Twenty-eight subjects (women: 8; age: 65 ± 10 yrs) completed treatment by ARAMIS; twenty-four patients (women: 11; age: 69 ± 7 yrs) completed a program of conventional rehabilitation and served as controls *(Figure 2)*. The patients' summary demographics and clinical records are summarized in *Table 1*.

The study was carried out in accordance with the Declaration of Helsinki concerning human studies (1960) and was approved by the Ethics Committee of the local health authority and by the Italian Ministry of Health and Social, Affairs Department for Innovation,
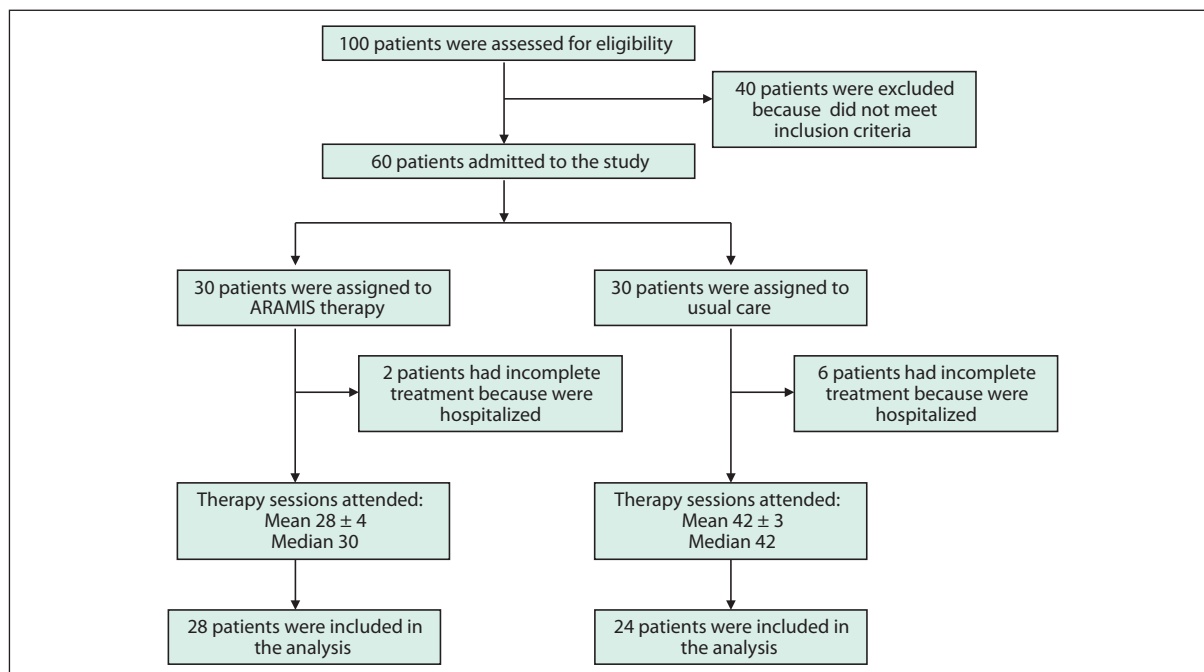

Figure 1
The ARAMIS model and experimental prototype.

Figure 2
Flow-chart of patient recruitment and assignment to the robot-assisted (ARAMIS) or conventional rehabilitation program.

Directorate-General Pharmaceuticals and Medical Devices (Code: ISA 200356). All patients were informed in full detail about the study purpose and procedures and gave their consent both for the rehabilitation protocol and the use of data, which were treated under conditions of anonymity.

Neuro-rehabilitation procedures

During the first week of hospitalization all patient were treated with same programs consisting of passive mobilization of upper and lower limbs, coordination respiratory exercises, cardiovascular conditioning in the setting posture, conditioning in the upright posture, exercises for the trunk control.

The robot-assisted and conventional rehabilitation programs are summarized in *Figure 3*. All patients also participated in the program of occupational therapy to promote recovery of autonomy in everyday life irrespective of the rehabilitation procedure (ARAMIS or conventional) to which they had been allocated. The ARAMIS protocol for rehabilitation included daily 60-min sessions over periods not exceeding 8 wks. Both single and multiple movements were planned; in the first 2-3 wks of treatment, all subjects performed a series of asynchronous exercises where the paretic arms repeated each of the exercises described as follows 20 times for a total of 200 repetitions per session:

basic exercises: Forearm pronation-supination; Elbow flexion-extension; Shoulder elevation: 30°, 60° and 90°; Shoulder abduction-adduction: 30°, 60° and 80°; Shoulder circling (circle movement on frontal axis); Shoulder flexion-extension.

functional exercises: Shoulder elevation 90° + Forearm pronation-supination; Shoulder elevation 90° + Elbow

Table 1
Demographic and clinical information upon admission

Demographic and stroke information	All patients n = 52	ARAMIS n = 28	Control group n = 24
Age, mean (SD), y	67 (9)	65 (10)	69 (7)
Days since stroke, mean (SD)	20 (8)	20 (6)	20 (10)
Side of stroke (R/L), n (%)	(24/28), (46/54)	(15/13), (53/47)	(9/15), (38/62)
Gender (M/F), n (%)	(33/19), (63/37)	(20/8), (71/29)	(13/11), (54/46)
Ischemic/Hemorragic, n (%)	(52/0), (100/0)	(28/0), (100/0)	(24/0), (100/0)
FM-score, mean (SD)	42 (16)	43 (18)	41 (13)
Motricity Index, mean (SD)	14 (5)	13,7 (5)	15 (6)
FIM, mean (SD)	60 (12)	58.6 (9)	61.3 (11)

SD: standard deviation; M: male; F: female; R: right; L: left; FM: Fugl-Meyer; FIM: Functional Independence Measures.

	WEEK 1	WEEK 2	WEEK 3	WEEK 4	WEEK 5	WEEK 6	WEEK 7	WEEK 8
ARAMIS Therapy Group	Baseline assessment •Upper limb posture in bed •Upper limb posture in wheelchair •Shoulder orthosis •Hand orthosis	Asynchronous exercises 200 repetitions/session		Asynchronous exercises 100 repetitions/session Synchronous exercises 100 repetitions/session			Asynchronous exercises 100 repetitions/session Synchronous exercises 100 repetitions/session Exercises in active-assisted modality Final assessment at discharge	
Control Therapy Group	Baseline Assessment •Upper limb postures in bed •Upper limb postures in wheelchair •Shoulder orthosis •Hand orthosis	•Passive mobilization •Neuromotor facilitation of shoulder muscles •Neuromotor facilitation of arm muscles •Neuromotor facilitation of forearm muscles •Neuromotor facilitation of hand muscles •Posture inhibiting pathological synergies		•Passive mobilization •Neuromotor facilitation of shoulder muscles •Neuromotor facilitation of arm muscles •Neuromotor facilitation of forearm muscles •Neuromotor facilitation of hand muscles •Posture inhibiting pathological synergies •Exercises to coordinate ocular-cephalic movements. Exercises of the "reach to indicate". Exercises of pre-configuration hand. Exercises of the "reach, touch, and manipulate". Coordination exercises proximal-distal. Grasping exercises. Exercises for manipulative skills and functional abilities. Exercises for the adaptation of the hand to the object without visual feedback. Exercises for the sensitivity. Biofeedback and electro-stimulation.			Final assessment at discharge	

Figure 3
Therapy programs with ARAMIS and conventional rehabilitation.

flexion-extension; Shoulder elevation 90° + Elbow flexion-extension + Forearm pronation-supination; Shoulder elevation 90° + 2 Elbow intermediate flexion-extension + Forearm intermediate pronation-supination.

In the following 2-3 weeks, the asynchronous exercises were progressively reduced to 100 per session and replaced by synchronous exercises (100/session), with the total number remaining unchanged. The sessions of rehabilitation in the active-assisted modality began following an adequate motor recruitment (if any) as documented in the Fugl-Meyer scale modified by Lindmark & Hamrin (total score > 70) to continue to the end of planned treatment *(Figure 3)*.

The traditional rehabilitation programs for the Control Therapy Group are described in *Figure 3*.

Outcome, tolerability and pain

The effects of treatment were blindly assessed by an independent rater. Ratings were at baseline and after completing the ARAMIS or conventional neurorehabilitation protocols by the Fugl-Meyer scale for the upper limb [21, 22], the Motricity Index [23] and the Functional Independence Measure [24-26]. The Fugl-Meyer scale version modified by Lindmark and Hamrin was preferred because it assesses both the motor disability and the underlying impairment. Subjective pain was tested by the Fugl-Meyer scale. The tolerability of the ARAMIS equipment and robot-assisted rehabilitative procedures was verified by the questionnaire developed by Krebs and co-workers [27].

Statistical analysis

Paired t-tests were used for assessing differences between patient groups within each time point. Mixed two-way ANOVA tests (one factor within and one factor between subjects) were used to contrast the progression of the two groups before and after treatment. Data normality was evaluated with the Shapiro-Wilk test.

RESULTS

The two patients groups did not present significant differences at admission for XXX (p-value > 0.05). The values of asymmetry and kurtosis indicate that the data are distributed normally, as confirmed by the Shapiro-Wilk tests (p > 0.05).

Patients undergoing treatment by ARAMIS completed 28 ± 4 sessions over a 54 ± 3.6-day period, for a total of 5600 ± 260 exercises. Single sessions were cancelled due to clinical or technical intercurring contingencies. Set-up and rehabilitation procedures were accepted by both therapists and patients, who tolerated the new approach without apparent or reported difficulties and appreciated being treated by a robot according to the questionnaire *(Figure 4)*. When subjective pain had already been reported upon admission, it improved at the end of treatment irrespective of the upper limb segment, whereas subjects reporting no pain at baseline never complained about it during or after treatment. The Fugl-Meyer subscore rates for pain of the ARAMIS subgroup were 3.25 ± 2.1 at baseline and 6.7 ± 1.6 after treatment (p < 0.001); those of the
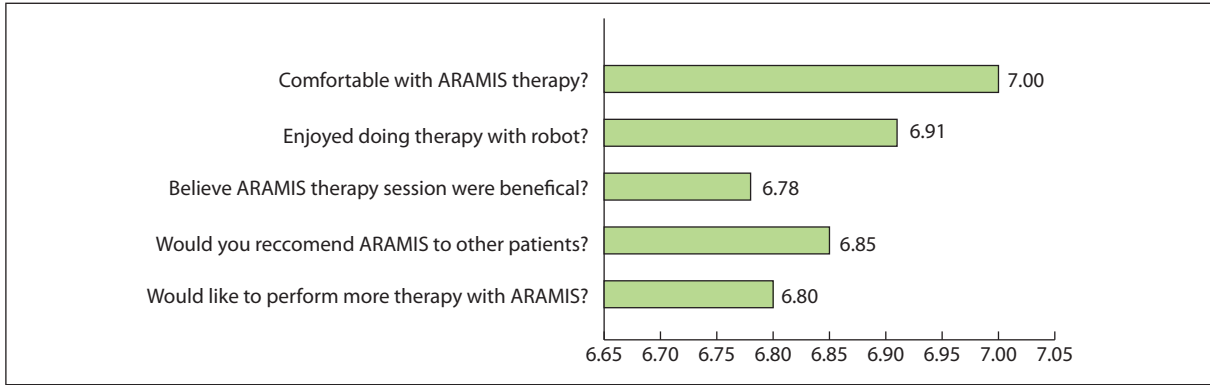
Figure 4
Tolerability of the ARAMIS equipment and rehabilitative procedures assessed by the questionnaire (Dijkers, 1991) [27].

control group were 4.1 ± 2.6 and 5.4 ± 1.9, respectively ($p < 0.05$).

The subgroup of patients undergoing rehabilitation by ARAMIS had an improvement in the Fugl-Meyer scale (global score: from 43 ± 19 at baseline to 73 ± 29 after treatment [$p < 0.00001$]), Motricity Index scale ($p < 0.004$) and Functional Independence Measure ($p < 0.001$). The Fugl-Meyer scores of the items for movements actively performed in the active-assisted treatment modality improved from 8.24 ± 3 to 22.7 ± 4.6 ($p < 0.0001$), with a 188.4% improvement. The Motricity Index for the upper limb and FIM also improved. The Fugl-Meyer global score of controls improved from 41 ± 13 at baseline to 58 ± 16 after treatment ($p < 0.006$) and the motor function item from 9.4 ± 4.1 to 14.9 ± 5.8 ($p < 0.023$) *(Figure 5)*. The motor improvement at the wrist and hand proved greater than at the shoulder and elbow irrespective of the treatment plan (ARAMIS

or conventional), but was greater in ARAMIS-treated patients than in controls *(Figure 5)*. The Fugl-Meyer global scores at baseline and after rehabilitation are reported for each patient in *Table 1*.

For the Fugl-Meyer scores, the mixed-ANOVA test rejected the null hypothesis that the two patient groups had an identical improvement over time ($p < 0.01$). This indicates that the treatment provided with ARAMIS is more effective than conventional therapy.

DISCUSSION

The ARAMIS project is aimed at developing robot-assisted rehabilitation procedures by supporting the processes that are thought to promote long-term plasticity after stroke and largely depend on the evolution of new motor skills [28]. Locomotion can recover also spontaneously through solutions that are kinesiologically improper, but functional [29]. However, the ef-
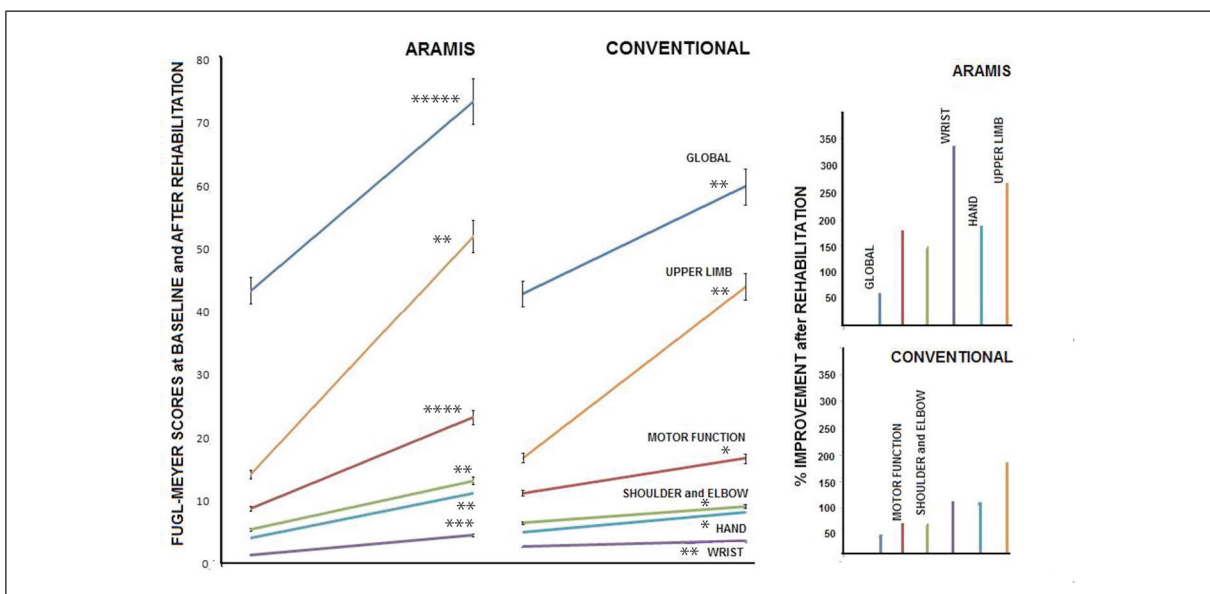

Figure 5
Global and partial scores of the Fugl-Meyer scale at baseline and after neurorehabilitation by ARAMIS or conventional therapy. Right: percent improvement from baseline. Statistical significance is indicated as *$p < 0.05$; ** $p < 0.01$; ***$p < 0.001$ **** $p < 0.0001$; ***** $p < 0.00001$.

fects of rehabilitation on the paretic lower limb are better and faster than those on the arm [30, 31], as the lower limbs functionally interact in hemiparesis after brain injury and the unaffected lower limb supports the paretic one [32, 33]. Conversely, the evolutionary role in the upper limbs in driving the subject's hands in the personal space under the control of vision [34] requires functional independence; for this purpose the motor system lateralizes early and contralateral control becomes progressively predominant while the ipsilateral one becomes functionally silent [28]. This arrangement is reinforced even only a few hours after stroke [35], which is partially due to compensation by the unaffected arm [36, 37]. As a result, the unaffected arm gains stronger independence than it would in physiological conditions and the paretic one is excluded when complex motor operations require bilateral coordination [38]. Only 30% to 66% of patients reach a satisfactory functional recovery of the upper limb [39-41]. Early [42] and late [43] rehabilitation with containment of the unaffected arm during intensive training of the paretic one has been suggested, but this is neither feasible nor tolerated by all patients.

ARAMIS is expected to promote the interaction between the paretic and unaffected upper limbs. The extent to which ARAMIS-assisted neurorehabiliation really results in such interaction remains to be documented in neuroimaging research with methodologies that can adequately describe brain plasticity and re-organization. However, the greater extent of motor improvement and recovery after robot-assisted compared with conventional neurorehabilitation [44-46] and the higher degree of improvement at the wrist/hand compared to the shoulder/elbow allow some inference. The exercises performed with assistance by a two-exoskeleton robot are intended to give priority to the rehabilitation of the proximal section of the arm; the results of this study suggest that the ARAMIS approach facilitates the mechanisms that regulate ipsilateral innervation and favor hand recovery. The effects of rehabilitation by ARAMIS on spasticity remain to be studied, although the improvement of pain suggests it is neither induced nor increased.

The master/slave exoskeleton functional organization that is peculiar to ARAMIS on the other hand allows a series of exercises to be planned in a variety that neither conventional rehabilitation nor robots with single exoskeleton structure can achieve. Furthermore, the intensity, accuracy and repeatability of training that are provided by ARAMIS and thought to favor recuperation [47-49] do not appear to be equaled by conventional treatments. Finally, the possibility to tailor the patient's movement with his/her motor anatomical/functional complexion as measured in the unaffected arm may

have been crucial in achieving a better recovery with ARAMIS than with conventional rehabilitation.

The application of advanced technology in medicine and rehabilitation is becoming widespread, and this is raising new issues about organization, staff, confidentiality and costs about which information is still lacking. However, the solution to these issues is key to bringing these promising systems into a stage of routine operation. There is a need for further research on the deployment of pervasive computing systems, including those transferring robomechatronic systems that are unfamiliar to the average patient and often poorly tolerated. This was not the case with ARAMIS, that was well accepted.

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