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"Translational Neurosciences and Neurotechnologies"

CYCLE XXXIV

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“SPINE FINE: a new software application for assessing the fine movements of the hands in patients with cervical spinal cord injury”

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INTRODUCTION

The annual prevalence of traumatic spinal cord injury (SCI) is now approximately 750 cases per million, and almost 50% of these cases occur at a cervical level. Spinal cord injury (SCI) has placed a formidable emotional, physical, and financial burden on people worldwide. Moreover, the weight-bearing and flexible nature of vertebrae at the cervical level make it particularly susceptible to injury. Clinical studies have shown that the incidence of cervical SCI in most countries ranges from 30 to 70 new cases per year, and lower cervical SCI (C3 to C7) accounts for approximately two-thirds of SCI with cervical fractures and three-quarters of SCI with cervical dislocations. Despite the massive impact of SCI, comprehensive treatment strategies aimed at reducing the initial degree of neurologic injury and improving the patient's functional capacity are lacking[1]. Paralysis after spinal cord injury (SCI) results in complex neuromuscular presentations due to wide ranges of severity, level of injury, and available activity-dependent rehabilitation. The functionality of the upper limb has a considerable impact on the quality of life of the patient with cervical SCI. In fact, 75–80% of these patients indicated that an important to very important improvement in the quality of their lives was related to an improvement in hand function. Approximately half of people with tetraplegia reported regaining arm and hand functions as the most important factor to improve their quality of life. More specifically Anderson reports that 48.7% of 347 people with cervical level SCI felt that gaining arm and hand function would significantly improve their quality of life and prioritized it over regaining sexual function, trunk stability, bowel and bladder control, and walking[2]. Similarly, Snoek reports that 77% of 565 people with tetraplegia in England and The Netherlands expected an important or very important improvement in quality of life as a result of improved hand function[3,4]. Therefore, attending to the incidence of the cervical SCI and the impact of the functionality of the upper limbs in their quality of life, it seems relevant to wonder about the evaluation, rehabilitation treatments, and future restorative approaches of the functionality of the upper limbs in tetraplegic/tetraparetic patients[5].

Scales for assessment of upper limbs function in cervical SCI patients

The most common method of arm assessment after cervical spinal cord injuries involves subjective ordinal scoring of motor function by a skilled examiner. The measures currently used most often in the SCI population are either too global in nature (incorporating the whole

body), are designed for different populations, assess a construct other than impairment of the upper limb, do not include sensory testing specific to the hand, or do not possess the psychometric properties required (*Table 1*).

***Table 1**. Outcome measures used for SCI and upper limb assessment*

Measure & Description	Construct & Population	Mode†	InR	ItR TrT	Construct Validity KG	ConcV	Res	Qualities‡
impairment								
International Standards of Neurological Classification of SCI (ISNCSCI)—classification measure, used to determine severity of injury[25,33]	whole body; pts w/ SCI	M	0.89–0.99					▲ ■ ♦
Grip and Pinch Dynamometry—measure of grip force[30]	hand strength; pts w/ peripheral hand injury	M	0.98§	0.99§				● ♦
International Classification for Surgery of the Hand—upper-limb motor strength test & 2-point discrimination of digits[31]	upper-limb motor strength; pts w/ tetraplegia	M						■ ● ♦
function								
Van Lieshout Test—upper-limb capacity seated in a wheelchair[36,45]	upper-limb function; pts w/ tetraplegia	M	0.98§			0.87 w/ Grasp & Release§	R§	▲ ■ ● ◘
Grasp and Release Test—functional test specific to ability after neuroprosthetic implantation[34]	hand function; pts w/ tetraplegia	M	0.87§					▲ ■ ● ◘
Capabilities of Upper Extremity Questionnaire—self-perception of functional ability w/ upper limbs (CUE)[29]	upper-limb function; pts w/ tetraplegia	SR	0.96§	0.94§		0.74 w/ FIM§		▲ ■ ● ◘
Jebsen Hand Function Test—generic hand function test w/ outcome of time[7,13]	hand function; pts w/ hand injury	M						● ◘
Sollerman Hand Function Test—hand function test[44]	hand function; pts w/ musculoskeletal conditions	M	0.98§				R	▲ ● ◘
Action Research Arm Test (ARAT)—upper-limb reach & grasp test[22]	upper-limb function; pts w/ stroke	M	0.92§	0.97§		0.81 w/ WMFT§		● ◘
Wolf Motor Function Test (WMFT)—hand function test[22]	hand function; pts w/ stroke	M	0.92§	0.97§		0.81 w/ ARAT§		● ◘
Fugl-Meyer Hand Subtest—hand function test[3,10,22]	hand function; pts w/ stroke	M	0.92§	0.97§		0.81 w/ ARAT§		● ◘
global function/independence								
Functional Independence Measure—generic outcome which measures burden of care[17,19]	independence; pts w/ any disabilities	O	0.70					
The Spinal Cord Independence Measure II (SCIM)—measure of global independence[5,12]	independence; pts w/ SCI	O	0.94§			0.79 w/ FIM§		▲ ■ ◘
Quadriplegia Index of Function—measure of global function[25,28]	independence; pts w/ tetraplegia	O						■ ◘
Lamb and Chan Questionnaire—ADL inventory specific to tendon transfer[21]	independence; pts w/ tetraplegia	SR						■ ● ◘

* ADL = activities of daily life; ConcV = Concurrent Validity; InR = Interrater Reliability; ItR = Intrarater Reliability; KG = Known Groups; M = clinician administers measure and rates individual; O = clinician observes activity of an individual and rates the individual; pts = patients; R = responsiveness established at acceptable level; Res = Responsiveness; SR = self-reported measure; TrT = Test-Retest Reliability.

† Mode is the manner by which the measure is administered.

‡ Qualities of the measure: ▲= psychometric properties evaluated with the SCI population; ■ = construct of measure specific to SCI; ● = construct of measure specific to the upper limb; ♦ = construct of measure specific to impairment; ◘ = construct of measure specific to function.

§ Interrater reliability above 0.8 intraclass correlation coefficient; intrarater or test-retest reliability above 0.8 intraclass correlation coefficient; concurrent validity above 0.7 correlation with a comparator measure, construct validity established.

Impairment of the upper limb is not the defined construct for any of the available measures. Although measurements of function and independence address very important clinical outcomes, they do not provide an understanding of neurological integrity, which underlies any change in level of function. The American Spinal Injury Association (ASIA) scale is the standard evaluation of the SCI patients; it includes muscle function grading, sensory grading, lesion level, and ASIA impairment scale (AIS). AIS is used to classify the patients in five main groups (A–E). It would be conceivable that upper limb functions should be related to the cervical lesion level and to the AIS[5]. The International Standards for the Neurological Classification of Spinal Cord Injury (ISNCSCI) exam is the standard clinical exam for

establishing the level and completeness of SCI and is most often utilized clinically as the primary outcome measure and designates the type of rehabilitation that will be offered to the patient. It has been designed to identify deficits in voluntary motor function and segmental sensation, in part through the motor, pin prick, and light touch scores. These scores have been shown to be valid and reliable indicators of the clinical status of SCI patients, in particular regarding motor and sensory deficits. However, the sensitivity and responsiveness of ISNCSCI motor scores to the complexities of paralysis within an American Spinal Injury Association Impairment Scale (AIS) classification and in response to activity-based therapy in chronic patients are limited[6]. On this field some authors suggest that the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI), the level of lesion, and the ASIA impairment scale are not linked with the functionality of the upper limb. It has been suggested also that other factors, such as strength, sensibility, or even the motivation of the patient, is more related to this functionality in the upper limb. The Jebsen-Taylor Hand Function Test (JTHFT) is a standardized measure for assessment of hand function that is reliable and valid for use with SCI subjects. The 9-Hole Peg Test (9-HPT) is a brief standardized and quantitative test of upper extremity function. Both JTHFT and 9HPT can be similarly used to quantify the functional impairment after cervical SCI. Moreover, both functional tests reflect the global strengths of upper limbs; the higher the motor score, the faster the tests execution. Some other tests are appropriate for the measurement of hand function in SCI patients, for example the Graded Redefined Assessment of Strength, Sensibility and Prehension (GRASSP) or the Capabilities of Upper Extremity Test, among others, but they cannot be completed in a short period of time[5]. Other SCI outcome measures such as the Functional Independence Measure (FIM) and the Spinal Cord Independence Measure (SCIM) to date have focused on the assessment of a patient's ability to perform a task using his or her remaining functional capacity. Thus, improvements on scales like these do not necessarily reflect neurological improvement and may actually measure to a greater extent compensated improvement. The Neuromuscular Recovery Scale (NRS) was developed within the NeuroRecovery Network (NRN) to provide a novel measurement tool addressing specifically the recovery of the neurological state after traumatic SCI and establish a classification scale focused on uncompensated task-specific recovery that can be used in clinical and research settings[6]. Therefore, in the past several years, only two assessments designed specifically for persons with tetraplegia due to cervical SCI have been developed: the Graded Redefined Assessment of Strength, Sensibility and Prehension (GRASSP) and the Capabilities of Upper Extremity Test (CUE-T). Both are reported to have good test-retest reliability and validity. These assessments were developed primarily for

clinical research, in order to be able to detect small but clinically meaningful changes in function. The GRASSP is a multidimensional assessment that includes strength, sensation, qualitative prehension, and quantitative prehension (QtP). The strength and sensibility components are impairment measures. The QtP scale is a capacity measure in the Activities domain, using the International Classification of Functioning, Disability and Health (ICF) framework, assessing what the individual can do in a standardized setting without equipment or assistance. The QtP-GRASSP evaluates different grasp patterns, but it allows item completion using an alternative grasp pattern, albeit with lower scores than if the expected grasp pattern is used. The CUE-T was developed using the Institute of Medicine model of disablement. It was designed to evaluate "functional limitation", which is a "restriction or lack of ability to perform an action or activity in the manner or within the range considered normal". Functional limitations operate at the level of the individual and reflect the combined impact of impairments on the actions a person can do without assistance or equipment. The CUE-T evaluates upper extremities actions such as reaching, lifting, pulling, and pushing in addition to various grasp patterns. Test procedures are designed to minimize the impact of functional limitations not involved in a particular test item. For example, a chest strap or trunk support can be used for the "lift up" item, leaning forward is not permitted for reaching, and items for grasp patterns are placed close to the subject to minimize the need to reach. In the CUE-T, grasping tasks must be completed using a designated grasp pattern; alternative grasp patterns are not allowed. The intent is to assess the action, for example "pick up something using tripod grasp pattern" not the task "pick up a pencil" [7]. Depending on the purpose of the assessment, one or the other test may be more appropriate. The CUE-T takes longer to perform than the QtP-GRASSP. In most cases it takes 40 to 60 minutes to complete the CUE-T, which is about twice as long as the QtP-GRASSP[7].

Quantitative evaluation of upper limbs function

Accurate and sensitive measurement of functional impairment is critical for determining the efficacy of treatments focused on restoring motor function. The most common methods of arm assessment after cervical SCI include subjective categorization of isometric force and free range of motion, like in the ASIA and GRASSP exams. These assessments use ordinal scoring, yielding rapid and reliable results, with scales designed to balance measurement sensitivity and reproducibility and consequently demonstrate excellent inter-rater reliability.

Nevertheless, they may not always be sensitive to small improvements that can be functionally meaningful. Sensor technology is capable of measuring motor function with greater precision, both because of a higher resolution scale and the capacity for a larger number of repeated trials within the same test session, and so numerous technologies have been developed to provide objective measurement of prehension. These latters may provide improved measurement sensitivity, and as sensor technologies have become smaller and more accessible, numerous tools have been developed for assessing arm function after cervical spinal cord injury. Dynamometers and myometers are widely used to measure isometric force of isolated arm functions in continuous physical units. Other assessment tools measure position and force during execution of simulated functional tasks. These systems indeed provide greater precision or a more direct characterization of functional ability than traditional measures, but the continued reliance upon ordinal assessment indicates an unmet clinical need for the development of measurement technologies[8]. To increase their utility and implementation, measurement systems should be simple to use, facilitate standardized administration, report sensitive, quantitative metrics, and provide reliable longitudinal testing. Grasse et al. designed a suite of modular rehabilitative devices for objective assessment of various isolated hand and wrist motor functions to address these needs. In addition to the measurement modules, a table-mounted armrest with simple, interchangeable tasks facilitates standardized administration across a wide range of arm impairments (*Figure 1*).

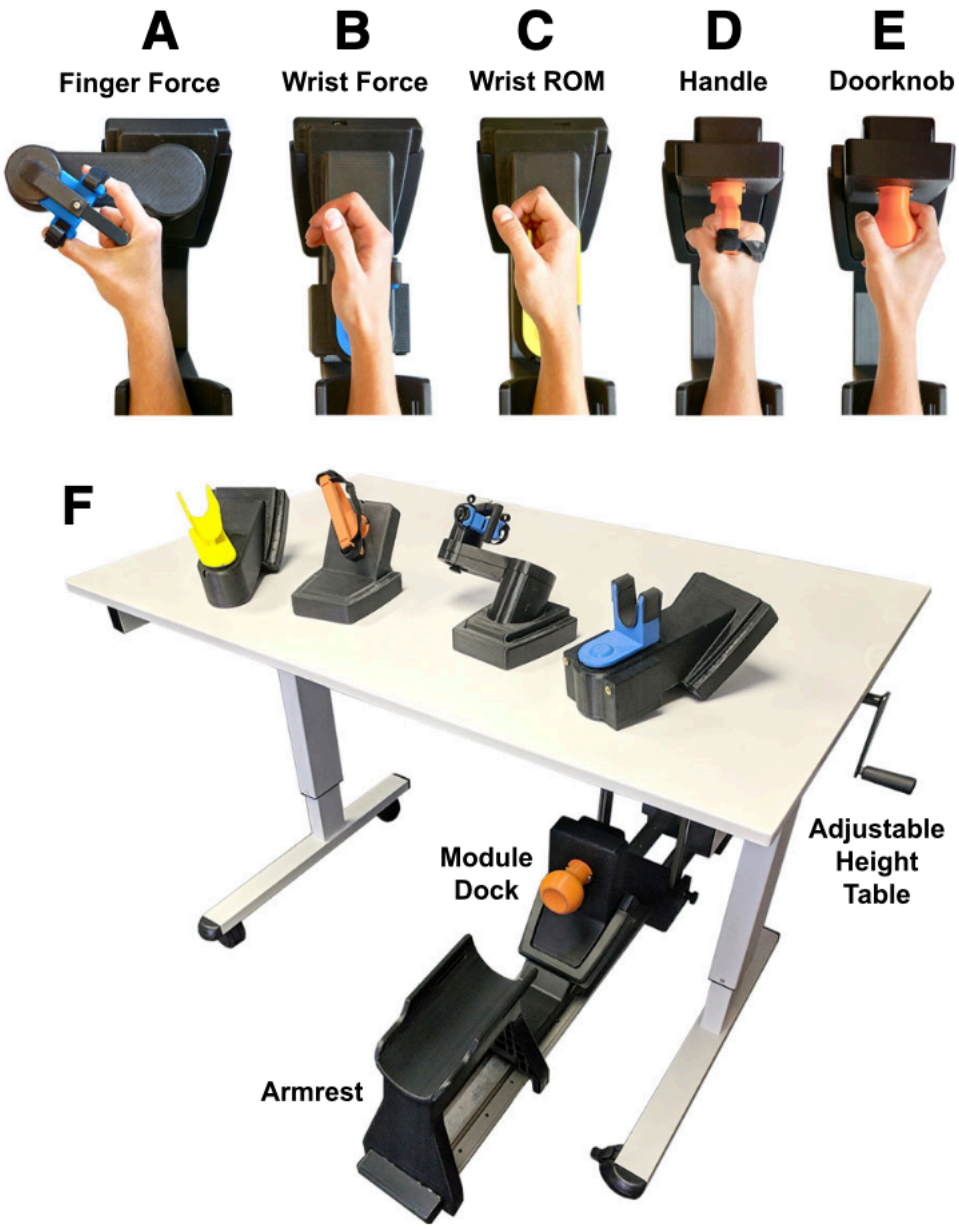


Figure 1*. Suite of hand and wrist assessment devices. Images of the finger flexion/extension device (**a**), the wrist flexion/extension devices (**b/c**), the wrist rotation device with the D-grip handle (**d**) and with the doorknob manipulandum (**e**), and the testing table used for assessing cSCI patients (**f**)*

The system records measurements in continuous physical units, providing unambiguous results across many aspects of function[8]. Furthermore, the devices enable collection of multiple trials to increase sensitivity and reliability of measurements. The authors tested whether these tools could quantify motor impairments in individuals with cervical SCI, determined measurement detection limits, and examined retest reliability by assessing the

same participants 4 months later. They established concurrent validity by correlating performance on the rehabilitative devices with two common metrics of upper limb function after cervical SCI, the Graded Refined Assessment of Strength, Sensibility, and Prehension (GRASSP) exam and the JTHFT. Their results demonstrated that the system provided reliable measurements over time and that performance were correlated with established outcome measures[8]. Confining measurements to a single degree of freedom of movement limits sources of error, helping to reduce variability and improve sensitivity. Following this rationale, Grasse et al. restricted their measurements to well-controlled movements that together require the majority of the muscles in the hand and forearm. Overall, the devices provided a robust characterization of impairments after cervical SCI. As expected, when compared to uninjured controls, cervical SCI participants were the most severely impaired on tasks that required finger strength[8].

Standard rehabilitation programs for incomplete upper limbs impairment

When from the first ASIA assessment a sensitive persistence is highlighted, in particular for pain sensitivity, it is possible to hypothesize a subsequent motor recovery that will be the more significant, the more important and rapid. Weak voluntary activities that do not progressively increase in the first few months often become useless when spasticity sets in. If the sub-injury motor recovery is minimal (as an elementary or isolated force) the injury can be considered functionally complete and therefore must be treated as such (obviously taking into consideration any benefits that even limited motor activity may entail for the patient). The main features of incomplete lesions are:

- the coexistence of voluntary motor activity and spasticity that hinders its expression, even if it can contribute to increasing the strength of a single muscle;
- absence or very limited presence of level lesion;
- the extreme variability of the possible clinical pictures due to the coexistence of different degrees of voluntary activity, spasticity and denervative phenomena (albeit partial);
- high frequency of centromedullary lesions, with more evident damage to the upper limbs than the lower ones.

The most frequent patterns of spasticity include:

- intra-rotated adducted shoulder;
- elbow flexed;
- forearm pronated;
- wrist and long fingers flexed;
- 1st finger in the palm.

Rehabilitation programs must remain flexible so that they can adapt to changes of the patient's neurological condition. Treatment is mainly aimed at balancing motor activity, reducing the spasticity of the prevailing districts and strengthening that of the respective antagonists; strengthening muscles that are already spastic can aggravate the imbalance. Whenever possible, functional movements should be stimulated avoiding excessive strain, because they can evoke greater spasticity. Therefore, the treatment of incomplete cervical SCI provides:

- passive mobilizations maintaining the full range of motion of the joints to preserve functional mobility;
- tendon elongation with slow and gradual stretching maneuvers necessary to maintain normal muscle length and to counteract muscle spasticity;
- inhibitory postures with positions contrary to those of the spastic muscle pattern;
- accurate positioning overnight;
- hydrokinesitherapy;
- reinforcement of the residual muscles through techniques that avoid that the strongest muscle groups dominate the movement, facilitating a motor pattern that is as normal as possible;
- Functional Electrostimulation (FES).

An integral part for the neurorehabilitation program of incomplete lesions are focal treatments with botulinum toxin and/or phenolic blocks. In fact, they allow both a period of rest to the antagonist muscles, which can be better activated, and at the same time the functional insertion of the gesture.

Standard rehabilitation programs for severe hands' impairment

When facing distal upper limbs impairment, the aim of the treatment is to recover the maximum functional capacity in order to improve autonomy or, in the most serious cases, to avoid complications from immobilization. The concept of maximum functionality passes through the research and preparation of compensating strategies. With the term compensations it is meant those strategies that the patient with tetraplegia/tetraparesis often spontaneously puts in place, to reach a functional goal that cannot be obtained according to conventional methods. The tetraplegic/tetraparetic patient often instinctively compensates motor deficiencies with alternative gestures that need to be known, both to be able to suggest them if necessary, and to treat the upper limb in order to facilitate them or at least make them possible. The most frequent compensatory gestures include joint freedom at the shoulder and elbow level. At the distal level, instead, the fundamental compensation is the “functional hand” in which the shortening of the flexors of the fingers and thumb compensate for the lack of voluntary grip. The goal that must be achieved, while ensuring complete joint excursion, is to produce the right muscle lengths of the hand to allow the "tenodesis effect" capable of reproducing a palm grip and a key-pinch grip through:

- shortening of the superficial flexors of the fingers;
- shortening of the intrinsics muscles of the hand;
- shortening of the long and opposing flexor of the thumb.

Therefore, with the wrist extended, the hand closes thanks to an active extension of the wrist or passively via forearm supination, while with the wrist flexed through active flexion or through relaxation, there is an opening of the fingers and an opening of the first space (thumb - index). In summary, the treatment must be aimed at:

1. correcting the management of range of motion and muscle tone;
2. strengthening of surviving or recovered motor activities;
3. training of useful gestures as soon as possible.

New strategies for rehabilitating upper limbs motor function

There is increasing evidence that motivating, intensive, and repetitive training can improve upper limb function after SCI. However, due to cost, as well as the monotony of hours of repetitive movements, therapists are limited in their ability to provide patients with motivating intensive training. Treatment options aiming to improve upper limb motor

functions are sparse; functional electrical stimulation and exercise are aimed at sensory-motor recovery, whereas other treatments offer functional gains with minimal or no effects on neurorecovery. For example, neuroprostheses and brain computer interface systems increase motor control through alternative communication and control systems, whereas reconstructive surgery of the upper limb offers permanent changes to muscle structure. There is evidence that repetitive and intensive practice can induce practice-dependent brain and spinal plasticity and that exercise intensity has a profound effect on sensory-motor recovery of patients with SCI. In this regard, rehabilitation robots hold promise for enhancing traditional physical and/or occupational therapy. They can deliver repetitive exercises at high intensities, for extended time periods, in a consistent and precise manner. In addition, real-time measurement of performance may provide advantage to therapists to modify the therapy protocol based on improvement in performance. In this context, some studies have reported that robotic-assisted rehabilitation can improve motor recovery after stroke and are safe and feasible in rehabilitation[3]. Therefore, rehabilitation robotics have contributed positively to the rehabilitation processes, speeding up recovery time, and reducing physical fatigue of the therapists. This has increased the interest in the development of medical devices for motor rehabilitation in the last decades. Particularly, several devices have been developed for upper limb rehabilitation such as exoskeletons and semi-exoskeletons devices. Exoskeletons and semi-exoskeletons devices offer large workspace and customizable exercises. However, they require large links, bulky frames, large motors and a precise axis alignment with the upper limb joints to avoid injuries. Furthermore, exoskeletons and semi-exoskeletons mechanism must be reconfigured to be used for both left and right arm or else an exoskeleton must be built for each human arm. Regarding portable mechanisms, they generally perform restricted trajectories limited by its mechanical structure. Although there are portable end-effector mechanisms that can reproduce customizable trajectories they require long links to cover most of the human arm workspace. Some cable driven devices offer convenient advantages regarding portability and customization of the exercises. However, the loss of tension of the cables when the patient makes an oppositional or involuntary movement is an issue that still requires further investigation. Furthermore, cable driven devices generally require to be over-actuated to keep the cable tension[9,10]. Another critical aspect regards some patients with SCI, who undergo a depression attack in the period following the injury. While a meta-analysis showed that exercise has a positive impact on depression, other studies have reported no positive impact on depression. Assuming that an exercise involving ambulation activities (e.g., body weight-supported treadmill training, overground training) would have a more positive impact on quality of life, there is probably a need for further exercises and

training programs targeted on arm ergometry and on fine movements of the hands, with the aim of recover even important gestures regarding everyday life[11]. Despite considerable interest in robotic gait training after SCI, very few reports have evaluated the effect of robotic training of arm and hand function in patients with tetraplegia/tetraparesis[3]. The virtual reality aspect of robotic therapy simulates real-life activities, provides encouraging feedback, and might motivate patients to endure more repetitions. Furthermore, such training might, according to the principles of motor learning, lead to improved functional outcomes. There have been several studies examining the functional outcomes of robotic training compared with the conventional training of the upper extremities. Some authors evaluated functional benefits of a treatment program developed to improve arm and hand motor functions and to assess tolerability and feasibility of a robotic device as an adjunct modality for upper limb rehabilitation in chronic, cervical SCI. The main study result has demonstrated that adults with chronic tetraplegia can benefit from intensive, repetitive training and that some improvement in arm and hand function was persistent at 6 months after the end of intervention. However, results should be interpreted with caution because the pilot study lacked a control group and had a small number of patients. Therefore, no conclusion should be drawn without a well-designed randomized controlled clinical trial. Nevertheless, on an individual basis, the results are encouraging for several reasons. First, all participants were at chronic stage of their injury. Second, research on arm and hand functioning in chronic, cervical SCI is relatively limited. Individuals with incomplete tetraplegia have residual motor function below injury level, and rehabilitation strategies should focus less on compensation and more on activity-based approaches to improve skilled movement performance. In the previous decades, both animal and human studies have provided sufficient evidence that sensorimotor function after SCI is enhanced by facilitation of neuroplasticity through functional training, and repetitive, intense training is the main factor in promoting such plastic changes in the central nervous system. The present results support the hypothesis that active repetitive movement of arm and wrist when coupled with exertion from the subject to overcome resistive forces produced by the robot may generate clinical benefits. On average, the number of repetitions gradually progress from approximately 200 repetitions on day 1 to approximately 1000–1500 on day 12. The progress is usually tailored to each subject's physical tolerance level for a given movement. Despite long training duration (3 hours of contact time with up to 60–70 minutes of active training time per limb), robotic-assisted training results feasible and highly tolerable (90%). Compliance with intervention protocol is at 100%. Subjects do not miss any therapy session due to excessive fatigue or soreness in upper limb or trunk/neck muscles. The task is easy, and the feedback

is useful to maintain motivation. In addition, there is no report of other adverse events related to overuse of musculoskeletal system such as severe pain or discomfort in the joints and surrounding soft tissue due to excessive forces acting upon shoulder girdle or elbow and wrist. In the case of Francisco et al. [3], the robotic device MAHI Exo-II is designed to fit well with anatomical joints and its passive degree-of-freedom along the longitudinal axes at wrist and hand enables easy positioning of various arm lengths. In addition, optimal positioning of subjects before training and constant monitoring during training is ensured (*Figure 2*).

***Figure 2**. Example of robotic device (MAHI Exo-II) during training (left) and target hitting task (right)*

An interesting finding is that after 4 weeks of intervention, gain from the repetitive training can be extended in overall arm function. The findings from these studies have shown that patients undergoing repetitive hand flexion/extension movement training showed improvements not only in the trained distal part of the limb (i.e., forearm and wrist movements) but overall, in the hand and arm activities. However, these activities were not translated into more complex function of arm and hand. In self-report, subjects required less assistance in activities such as lower body dressing, picking and releasing small objects, grasping, hugging, and turning pages[3]. In a Cochrane review by Mehrholz et al., 34 trials of persons with stroke receiving robotic training were included[12]. The persons receiving robot-assisted therapy were more likely to improve their arm strength and arm function than the

control groups that received conventional therapy. Nevertheless, robotic-based training programs present some limitations regarding the scarce user-centered design, the long set up time, the need for a special space where to install the robot and the obligation for the patient to go to the rehabilitation center equipped with the robot whenever he wants to practice, thus not maximizing the possibility of using such technology[13].

Software application for assessing fine movements of the hands

The advantage of using tools for the assessment of neurological and functional deficit of the upper limbs in patients with cervical SCI and their importance in integrating the assessment scales commonly used in clinical practice, and inevitably influenced by operator-dependent biases, has been already documented. Herein we propose the possibility of administering tasks for the impaired hands through touchscreen devices, using a dedicated software application capable of objectively reproducing and evaluating some of the common hand gestures of everyday life, quantifying the correctness in the execution of the task, the time taken for its completion, and the degree of precision. The aim of the application is to furnish important supplementary information regarding both the effectiveness of the surgery performed, the rehabilitation path to set up and its impact on patients' outcome. Compared to traditional evaluation scales, the application provides additional, quantitative and standardized data, not operator-dependent, through the analysis of tasks that reproduce hand gestures normally performed in daily life and therefore more reliable in terms of functional evaluation of distal movements of the upper limbs. From the recent evidence reported in the literature, it would emerge that, particularly in the area of fine movements of the hand, a detailed pre- and post-operative classification of the deficit would allow for tailored neuro-rehabilitation programs. The aim of our prospective study is to calculate the concordance between the scores of the evaluation scales currently in use and the information provided by the application (tasks' accuracy percentage and tasks' execution time) in terms of impairment of fine movements of the hands. In particular, the measurement of functional outcome at the end of rehabilitation will allow to verify whether, in patients who have not achieved optimal results, the additional information provided by the application would have suggested an adjustment of the therapeutic protocol. The secondary objective consists in evaluating the usefulness and the possible impact of the repetitive execution of the tasks administered by the application as potential training exercises during the rehabilitation program for the recovery of fine movements of the hands.

MATERIALS AND METHODS

Study design, patients' sample and inclusion criteria

Four different centres will contribute to the present prospective study: two trauma centres ("C.A. Pizzardi" Maggiore Hospital of Bologna and "M.Bufalini" Hospital of Cesena), one university hospital (Arcispedale S.Anna – University Hospital of Ferrara), and one rehabilitation institute (Montecatone Rehabilitation Institute). Patients aged 18-75 years with cervical SCI needing for surgery will be prospectively collected by the Spine Division of Maggiore Hospital (Bologna), the Neurosurgery divisions of Bufalini Hospital (Cesena) and S.Anna University-Hospital (Ferrara), and by the Spine Unit of Montecatone Institute, with this latter representing the only division dedicated to the post-surgical rehabilitation program for all the patients with cervical SCI included in the study. The administration of the tasks of the application will be integrated to the clinical and neurological evaluation in those patients treated in the hospitals of Cesena and Ferrara (*study group*), while the patients treated in the hospital of Bologna will be evaluated with the current scales for assessing the upper limbs impairment (*control group*). Patients with cognitive impairment, intrinsic hand dysfunction, complete tetraplegia (ASIA A) or other comorbid neurological disease will be excluded, together with patients with AOSpine fracture types A1, F1, and F2 (not needing surgery), patients without neurological impairment (ASIA E), polytraumatized patients or patients with other spinal fractures, and patients with previous surgery for degenerative or traumatic diseases of the cervical spine (*Figure 3*).

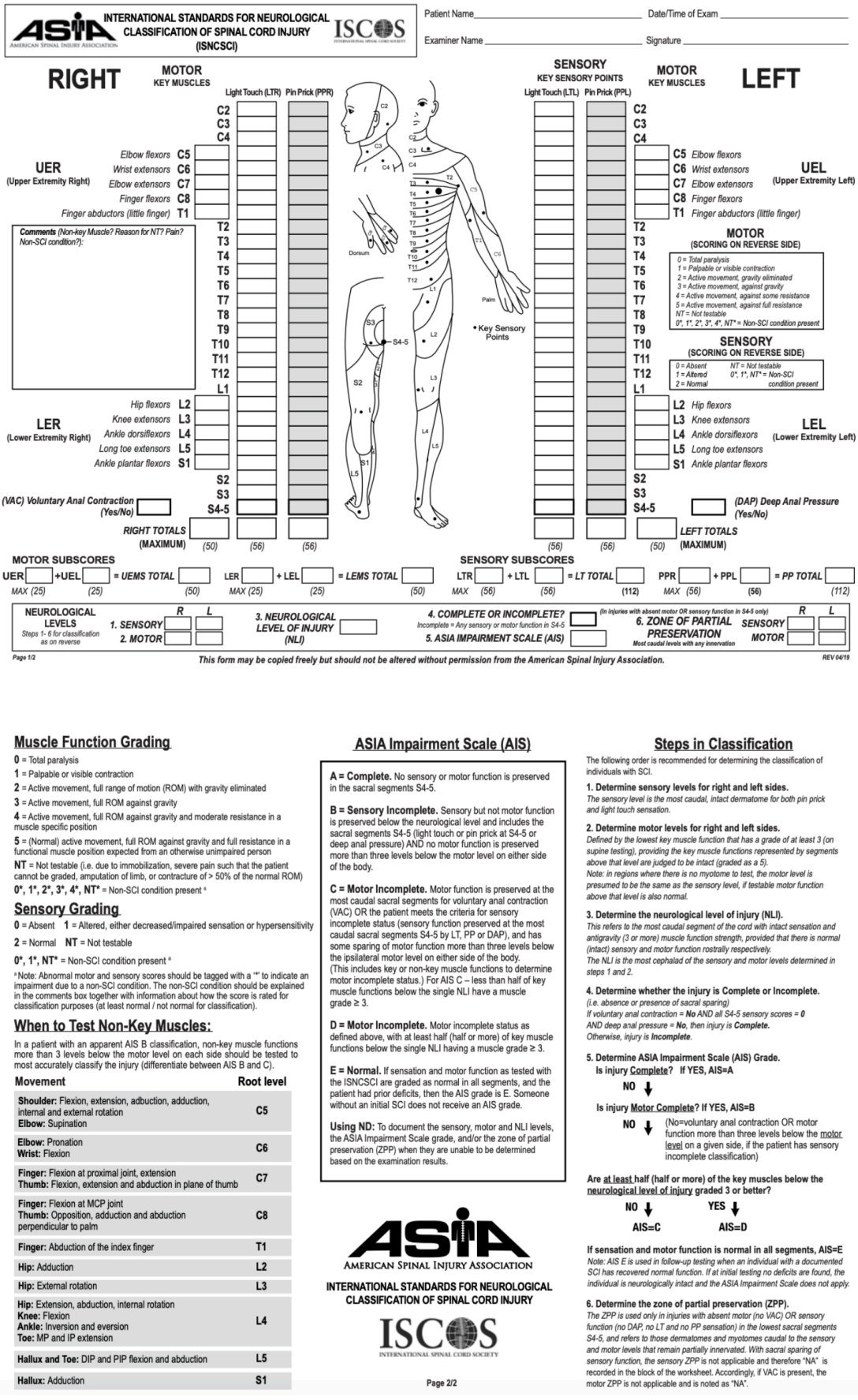


Figure 3. *ASIA Score for the assessment of neurological impairment*

All patients diagnosed with cervical SCI with type A2, A3, A4, B1, B2, B3, F3, and F4 cervical fractures according to the AOSpine Classification System, thus requiring surgery, will be considered eligible for the study (*Figure 4*).

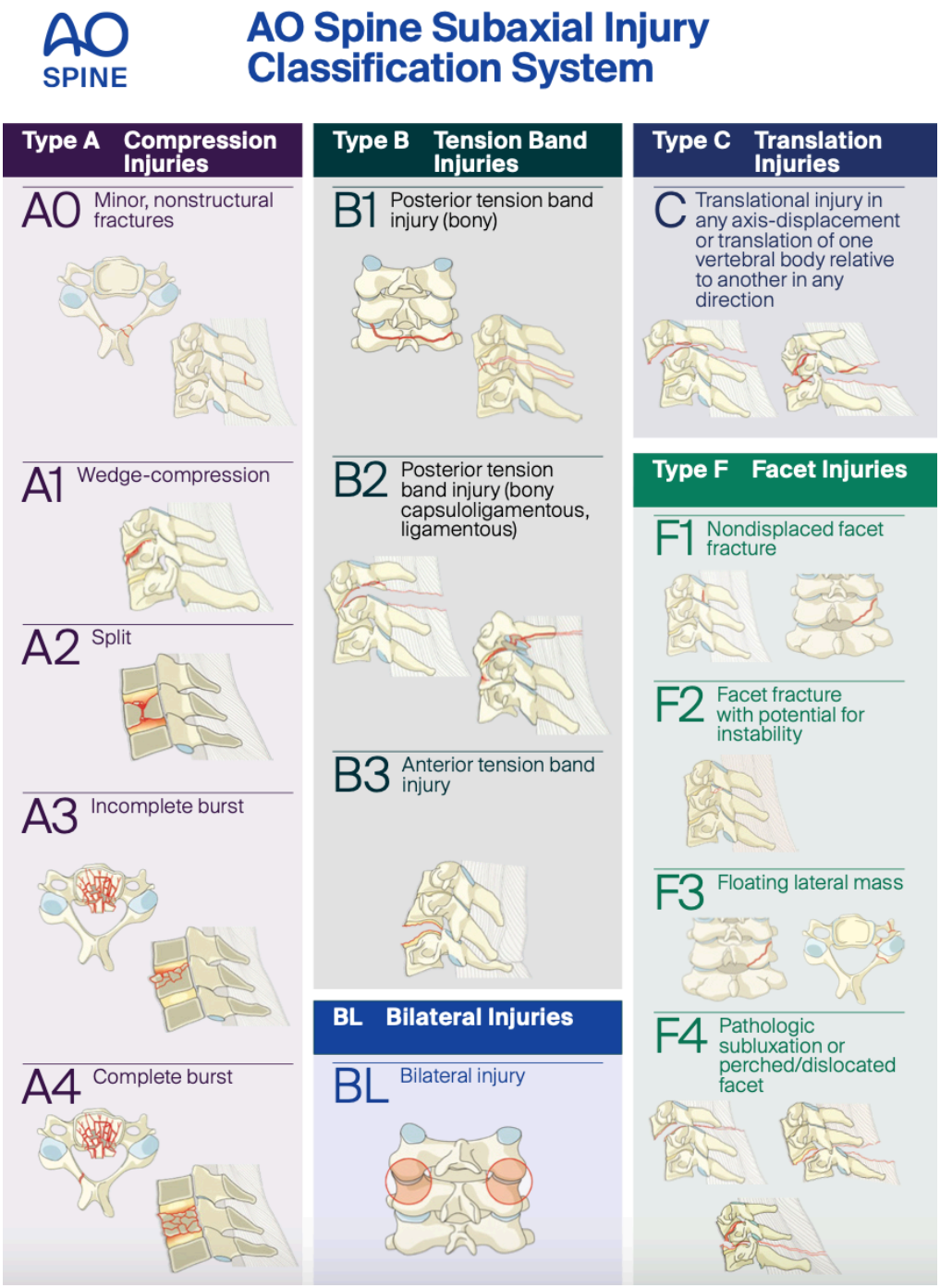


Figure 4. *AOSpine Subaxial Injury Classification System for assessment of traumatic injury of the cervical spine*

All the aspects of this study protocol have been already approved by the institutional review boards of the centers of Cesena and Montecatone prior to patient's enrollment. The

applications for the ethics committees of Bologna and Ferrara are also in the process of being submitted. Informed consent for study enrollment will be obtained from all patients.

Analogic and digital hand testing and functional outcome

Compatibly with age and general clinical conditions, the application tasks will be administered in addition to the evaluation scales and neurological examination normally recorded during the current clinical practice. At the admission, ASA, ASIA score, modified Rankin scale (mRS-pre) and Charlson Comorbidity Index (CCI) will be evaluated. Questionnaires with new modified Rankin scale (mRS-post/-post6/-fup), Neck Disability Index (NDI-post/-post6/-fup) and Smiley Webster Pain Scale (SWPS-post/-post6/-fup) will be administered at 1 (-post), 6 (-post6) and 18 months (-fup) from the end of the treatment to estimate the functional outcome in terms of general disability, disability related to the cervical spine and ability to return to work / previous activities. ASIA score with Muscle Function Grading, GRASSP test for assessing strength, sensation, and qualitative prehension (*Figure 5*), and 9-HPT (*Figure 6*) to evaluate upper extremity dexterity will be administered before and after the surgical procedure and during the neurorehabilitation process, as per current clinical practice, recording the results at 1, 6 and 18 months after trauma.

TEST GRASSP

Graded Redefined Assessment of Strength Sensibility and Prehension (GRASSP)

SCORING SHEETS

1 - Demographics

Patient Name	
Examiner	
Assessment Number	1 2 3 4 5 6
Date of Assessment	
DOB	
Gender	
Hand Dominance	
Pre-injury	
Post-injury	
Injury Date	
Injury Type Brief Description	
Surgery/Intervention and Date	
Comments	

2 - Strength - score 0 to 5 as per instructions in each box, then sum for each side

Right	Muscles Tested for MMT	Left
	Anterior Deltoid	
	Elbow Flexors	
	Elbow Extensors	
	Wrist Extensors	
	Extensor Digitorum (DIII)	
	Opponens Pollicis	
	Flexor Pollicis Longus	
	Finger Flexors (DIII)	
	Finger Abductors	
	First Dorsal Interossei	
/50	**Total out of 50 for each side**	/50

3 – Sensibility

SWM Threshold Scores																
Right Hand									Left Hand							
3.61 (4)	3.61 (4)	3.61 (4)	4.31 (3)	4.56 (2)	6.65 (1)	NR (0)	Score	Area	3.61 (4)	3.61 (4)	3.61 (4)	4.31 (3)	4.56 (2)	6.65 (1)	NR (0)	Score
								1								
								2								
								3								
Dorsal Total							/12		Dorsal Total							/12
								4								
								5								
								6								
Palmar Total							/12		Palmar Total							/12
Dorsal Total+Palmar Total=Total SWM							/24		Dorsal Total+Palmar Total=Total SWM							/24

4 - Prehension

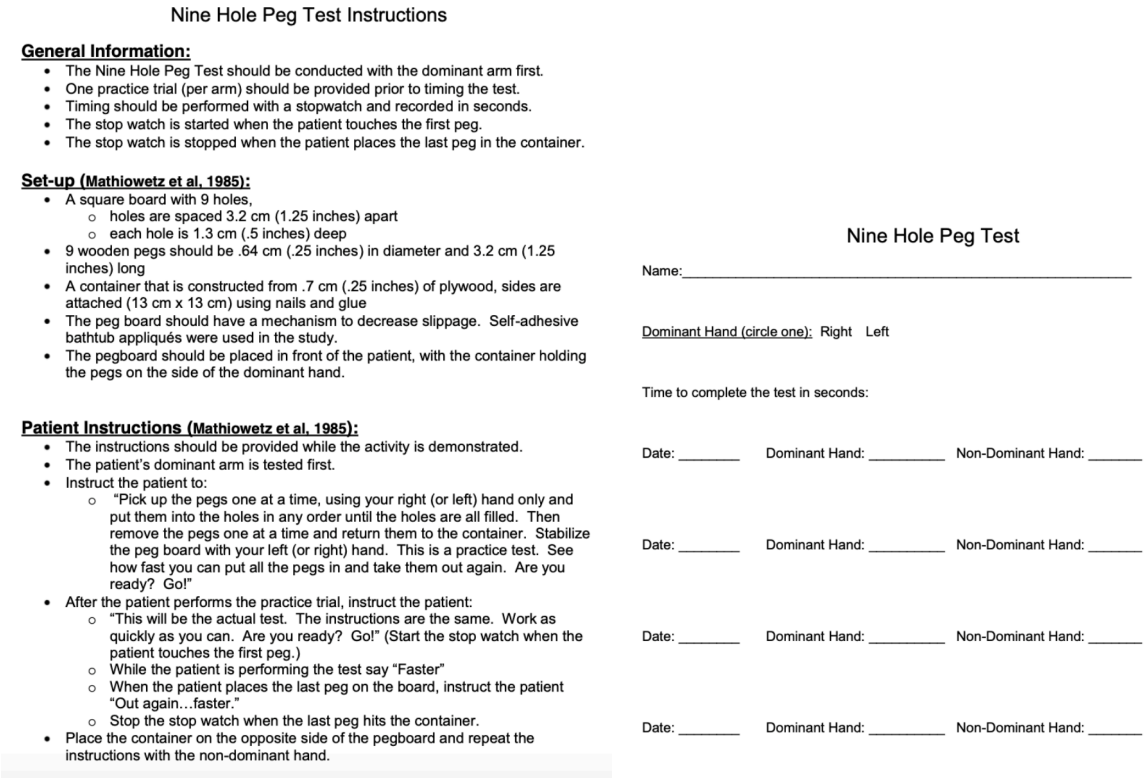
A - Qualitative Prehension

Right	Qualitative Grasps	Left
	Cylindrical Grasp	
	Lateral Key Pinch	
	Tip to Tip Pinch	
/12	**Total out of 12**	/12

B - Quantitative Prehension

Right			Task/ Instruction Expected Prehension	Left		
Time	Score	Drops		Time	Score	Drops
			1. Take the bottle and pour the water into the cup, approx. ¾ full. Cylindrical grasp			
			2. Unscrew the 2 lids of the jam jars and put them onto the table. Spherical grasp			
			3. Pull the 9 pegs, one by one, out of the foam and stick them back into the markings on the opposite side. Tip to Tip pinch			
			4. Take the key from the table, insert it in the lock and turn it 90°. Lateral Key pinch			
			5. Pick up the 4 coins, one by one, from the table and put them through the slot. Tip to Tip Pinch			
			6. Pick up the 4 nuts, one by one, from the table and screw them on the matching screws. Tip to Tip pinch and/or Tripod pinch			
			Total Score /30			

Figure 5. *GRASSP test for assessing strength, sensation, and qualitative prehension*



Nine Hole Peg Test Instructions

General Information:

- The Nine Hole Peg Test should be conducted with the dominant arm first.
- One practice trial (per arm) should be provided prior to timing the test.
- Timing should be performed with a stopwatch and recorded in seconds.
- The stop watch is started when the patient touches the first peg.
- The stop watch is stopped when the patient places the last peg in the container.

Set-up (Mathiowetz et al, 1985):

- A square board with 9 holes,
  - holes are spaced 3.2 cm (1.25 inches) apart
  - each hole is 1.3 cm (.5 inches) deep
- 9 wooden pegs should be .64 cm (.25 inches) in diameter and 3.2 cm (1.25 inches) long
- A container that is constructed from .7 cm (.25 inches) of plywood, sides are attached (13 cm x 13 cm) using nails and glue
- The peg board should have a mechanism to decrease slippage. Self-adhesive bathtub appliqués were used in the study.
- The pegboard should be placed in front of the patient, with the container holding the pegs on the side of the dominant hand.

Patient Instructions (Mathiowetz et al, 1985):

- The instructions should be provided while the activity is demonstrated.
- The patient's dominant arm is tested first.
- Instruct the patient to:
  - "Pick up the pegs one at a time, using your right (or left) hand only and put them into the holes in any order until the holes are all filled. Then remove the pegs one at a time and return them to the container. Stabilize the peg board with your left (or right) hand. This is a practice test. See how fast you can put all the pegs in and take them out again. Are you ready? Go!"
- After the patient performs the practice trial, instruct the patient:
  - "This will be the actual test. The instructions are the same. Work as quickly as you can. Are you ready? Go!" (Start the stop watch when the patient touches the first peg.)
  - While the patient is performing the test say "Faster"
  - When the patient places the last peg on the board, instruct the patient "Out again…faster."
  - Stop the stop watch when the last peg hits the container.
- Place the container on the opposite side of the pegboard and repeat the instructions with the non-dominant hand.

Nine Hole Peg Test

Name:_____

Dominant Hand (circle one): Right Left

Time to complete the test in seconds:

Date: _____ Dominant Hand: _____ Non-Dominant Hand: _____

Date: _____ Dominant Hand: _____ Non-Dominant Hand: _____

Date: _____ Dominant Hand: _____ Non-Dominant Hand: _____

Date: _____ Dominant Hand: _____ Non-Dominant Hand: _____

Figure 6. *Nine-Hole Peg Test (9-HPT) to evaluate upper extremity dexterity*

In each evaluation the patient will seat with their shoulder adducted, elbow flexed, forearm neutral, and feet resting on the ground. The dominant hand will be tested first, followed by the nondominant hand. The patient will perform the GRASSP and the 9-HPT tests twice with each hand, and the scores averaged for each hand. In addition to these assessment scales, the application tasks will be administered to the patients in the *study group* before and after the surgical procedure and during the clinical follow-up at 1, 6 and 18 months. Moreover, at the beginning and at the end of the neurorehabilitation program, all patients will be subjected to a muscle excitability test (Neurotech., 30hz – 300μs at maximum intensity), which allows to evaluate the concomitance of a central lesion and a cervical lesion and their relative amplitude. Such test, limited to the deltoid, biceps, triceps muscles (to assess whether they are inactive or deficient) and the radial, median and ulnar nerves, evaluates the extent of the level lesion and the muscular imbalances that the patient may suffer, thus providing information on the methods of treatment and on their impact on outcome.

Software application

The application, called "SPINE FINE", developed from September 2020 to September 2021, will administer the following exercises to the patient through an iPad: completion of geometric figures of decreasing sizes (square, triangle, pentagon each of 3 sizes), their subsequent reproduction with respect to a model presented on one side of the screen, the writing of words, drawn from the app among the 1000 most used words in the Italian/English vocabulary, within predetermined spaces, and the tracing of a path through increasingly narrow labyrinths of 3 different sizes. Each of the aforementioned tasks, grouped as "tracing tasks", will be performed even with the Apple Pencil by patients able to hold this tool (*Figure 7 – 10*) and the tracing performance will be evaluated in terms of accuracy percentage, thus indicating with 100% the perfect execution of the task.

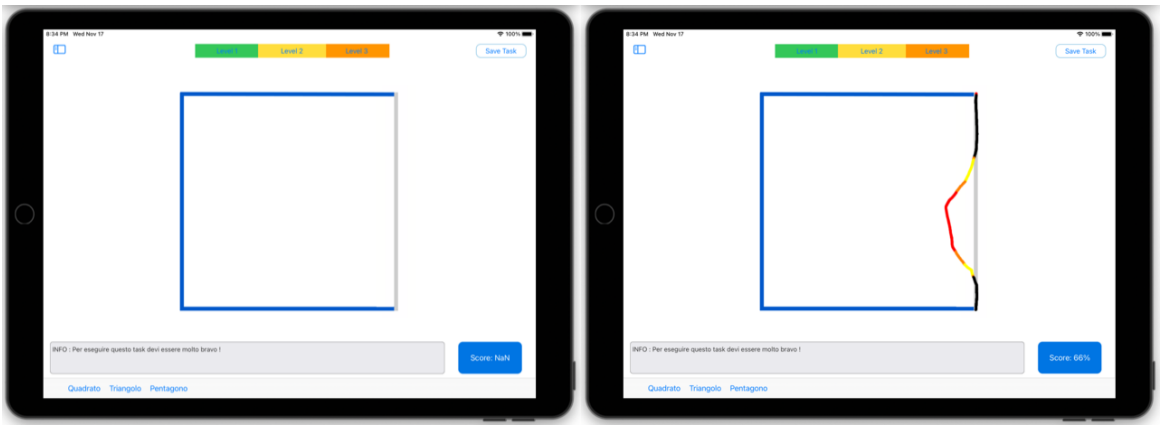


***Figure** 7. Draft of the task of completing the figure. On the right an example of a tracing error, whose severity is marked with a color-code and calculated in terms of accuracy percentage*

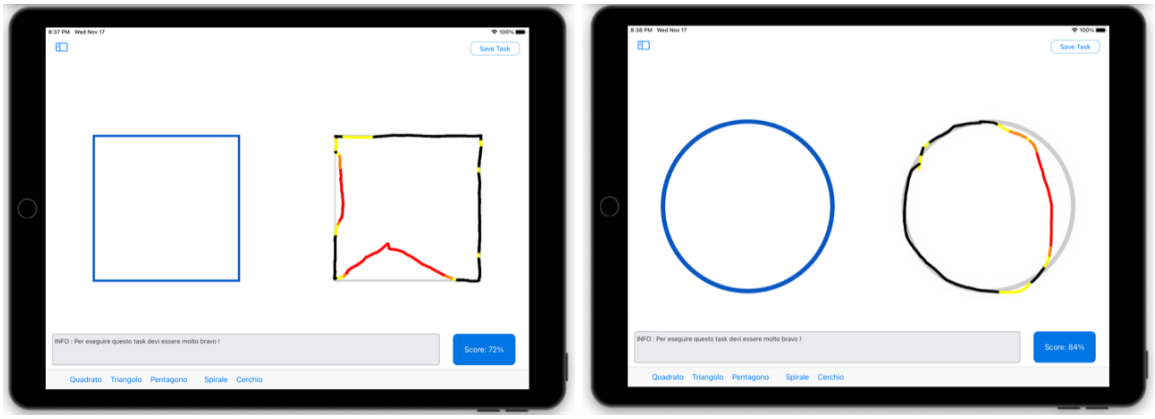


Figure 8. *Draft of the task of reproducing the figure. Examples with tracing errors, whose severity is marked with a color-code and calculated in terms of accuracy percentage*

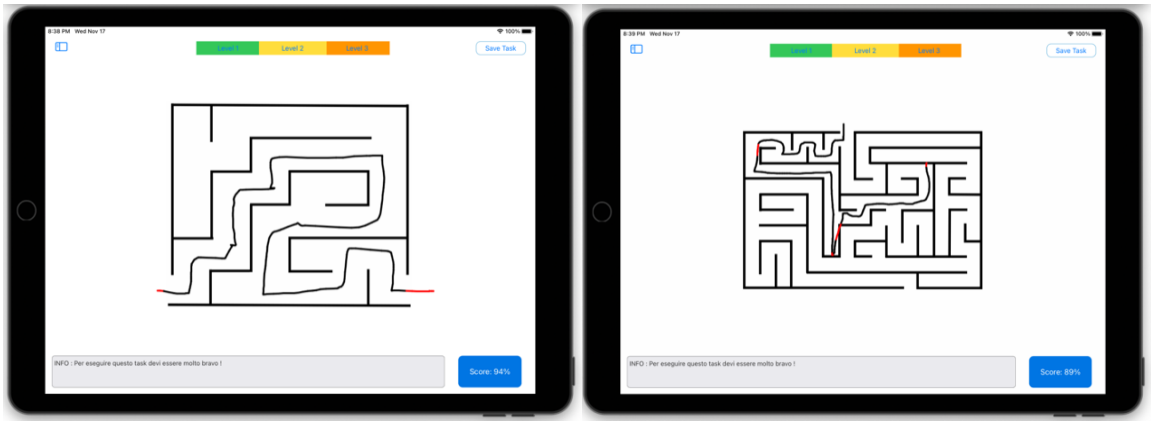


Figure 9. *Draft of the tracing tasks within labyrinths with increasingly narrowing paths. Examples of tracking errors from contact with path boundaries marked with a color-code and calculated in terms of accuracy percentage*

Figure 10. *Draft of the task of writing words inside predetermined spaces of decreasing size with tracing overruns highlighted by a color code and calculated in terms of accuracy percentage*

The application will then administer "multifinger tasks" to evaluate the coordination of each hand through exercises requiring the contemporary use of two or three fingers: dragging two and then three balls with two and three fingers in a predetermined position, zooming in/out figures with thumb-index and thumb-middle finger up/down to the size of the figure proposed by the application (mimicking pinching), orient, rotate and drag figures with two and three fingers (replicating movements such as that to unscrew a cap or to rotate a key in a lock) until they fit into the space proposed by the app. For multifinger tasks the app will stop the dragging, zooming and rotation of the figures if it identifies the loss of contact of one or more fingers from the screen. For these exercises it will be sufficient for the app to evaluate the execution time of the tasks to estimate the patient's performance, since the error, given by the loss of contact of the finger with the screen, will cause an interruption of the task with a consequent slowdown in its accomplishment (*Figure 11 – 13*).

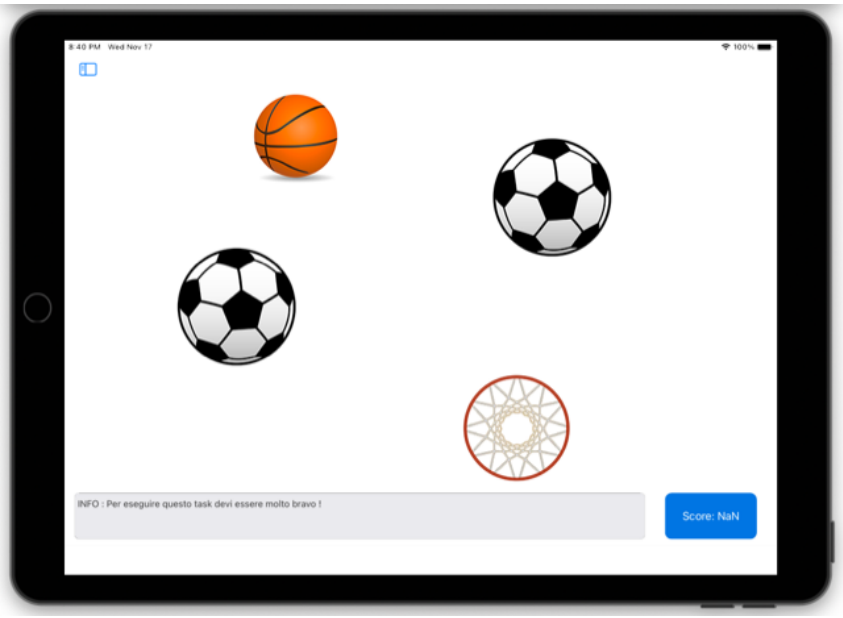


Figure 11. *Draft of the task of dragging two and three balls with two and three fingers in a predetermined position (centering the basket with the appropriate ball), never losing the contact with the screen*

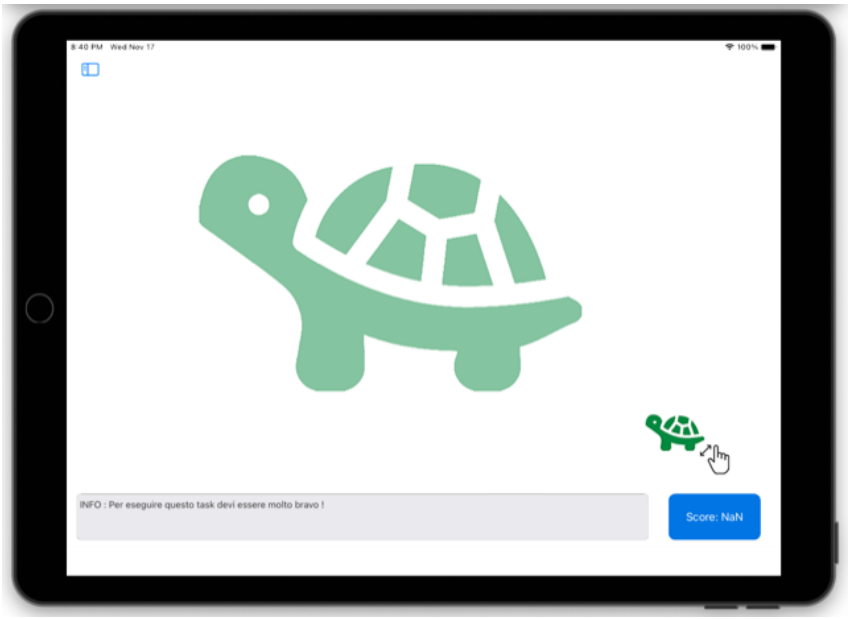


Figure 12. *Draft of the task of zooming in/out figures with thumb-index and thumb-middle finger up/down to the size of the figure proposed by the application*

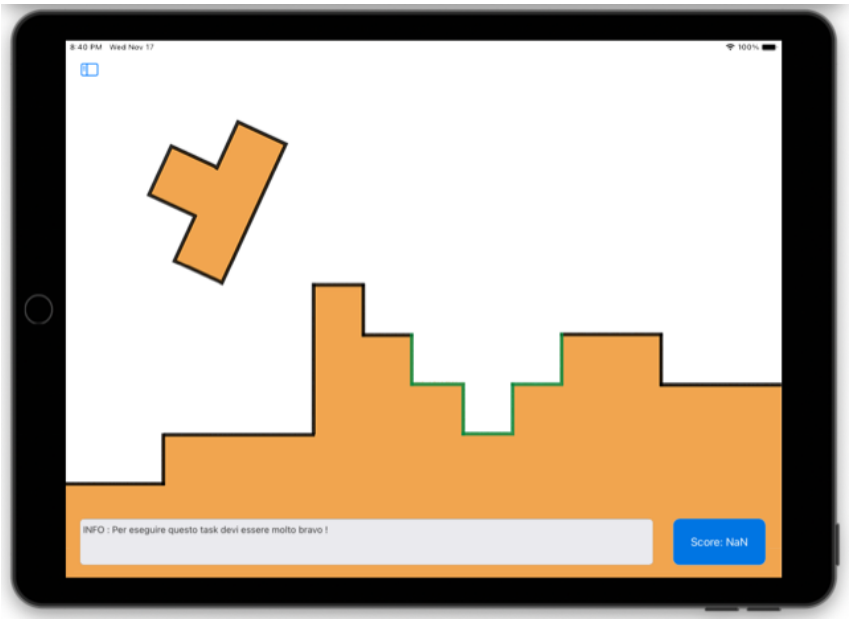


Figure 13. *Draft of the task of orienting, rotating and dragging figures with two and three fingers until they fit into the highlighted space*

At the start of each task, the application will provide instructions on how to execute it correctly through a banner both in Italian and English at the bottom of the screen, which can be recalled by the user even during the execution of the task, through a special icon. The application will make possible to calculate the execution time and the percentage of errors with respect to the ideal tracing, which will be performed both with the fingers and with the Apple Pencil. The user will be able to perceive in real time the degree of error through the accuracy percentage showed on the screen at its bottom right and through a color code that will make the drawn line progressively yellow, orange or red, the more the line will move away from the suggested tracing. Each patient will be assigned a random alpha-numeric code generated at the end of the execution of the tasks administered. The application will then produce a report on .pdf file for each patient at the end of the assessment session with the overall error rate and for the individual tasks, with their respective execution times, without storing any tests or data attributable to patients. Therefore, no data will be recorded, since the task analysis report will be transcribed only in the final .pdf file which, if not saved on an external archive, will be automatically deleted when it is closed. The report data will then be collected in anonymized form, reporting the patient's code via a web-based Collection Card (e-CRF), stored in a central computerized database and the .pdf report deleted. To access the e-CRF each Investigator must use their personal login credentials (user-id and password). The credentials are nominative and linked directly to the Investigator not to the

center. Each center authorized to use the platform will only be able to access the data of its patients. Access to information by individual Centers (registration / consultation of data) will take place via the internet in a secure manner, using the HTTPS protocol (through which the information will be encrypted). Data collection fully complies with the current Privacy Law (EU Regulation GDPR 2016/679) and each patient will have given their informed consent to the processing of individual data.

Application score

Regarding the automatic evaluation of the results, the app takes care of assigning a score through weighted average on error levels (distance from the ideal solution) for tracing tasks. In particular, the system is divided into bands of 20 pixels associated to colors:

- divergence within a max of 20 pixels = yellow error
- divergence in the interval 20 < x <40 pixels = orange error
- over 40 pixels = red error.

Scores are calculated according to the formula:

$$Pt = 1 - (R + O / 2 + Y / 4) / (N + R + O + Y)$$

Where R are the Red points, Y the Yellow points, O the Orange points, and N the black strokes (the correct ones). As regards the evaluation of multifinger tasks, the score is represented by the time taken to perform the task, expressed in seconds and calculated from the start of the movement for reaching the goal.

Statystical analysis

The statistical analyses will be performed with the Statistical Package for Social Sciences for Windows (SPSS Inc. Released 2008. SPSS Statistics for Windows, Version 17.0, Chicago, IL, USA). The descriptive statistical analysis will consider age, Charlson Comorbidity Index, ASA score, ASIA score, modified Rankin Scale pre-treatment, AOSpine classification, fractured vertebra, type of surgical treatment, duration of neurorehabilitation pathway, GRASSP test score, “nine-hole peg” test score, application test

scores. The outcome variables will be analyzed: complications, radiological outcome, post-treatment ASIA score, Neck Disability Index, modified Rankin Scale, Smiley-Webster Pain Scale, manual muscle test score, GRASSP test score, nine-hole peg test score, and application test scores. Agreement will be measured by Cohen's K. Results showing a $p \leq 0.05$ will be considered statistically significant.

EXPECTED RESULTS

Application timetable

The development project of SPINE FINE was approved and funded entirely by the Nuvasive company on 09/21/2021 through its Corporate Grant Program (GrantID1466). The loan was therefore disbursed by Nuvasive Italia to the Principal Investigator and creator of the app (Giorgio Lofrese) through the Montecatone Foundation. The study protocol, designed as a no-profit, provides for the support of the SPINE FINE application to the current methods of evaluating fine hand movements. It was approved by the Ethics Committee of AUSL Romagna on 08/10/2021 (prot. 8525/2021 - I. 5/233) and it has just been submitted to the ethics committees of the other centers included in the study. The free release of the application on the Apple Store, in beta version, is expected for December 2021, then the start of its use for January 2022. After fixing any eventual bug, by February 2022 the application will be available in its final version and, in September 2022, a recruitment campaign will be activated for the major trauma centers in Europe with the aim of promoting the use of the application and therefore a data collection, as broad as possible, useful for interpreting in the most objective way the numerical parameters produced by the app. Starting from the 4 centers involved in the study, we estimate to be able to enroll between 40 and 50 patients per center per year, for a total of about 160 patients in the first year. After having analyzed and published the preliminary data, extending the network of centers with a recruitment campaign, we are confident of being able to include approximately 700 patients in an European multicentric study by February 2024 (*Table 1*). With such a large sample size we expect to be able to correlate the data recorded by the app with the evaluation scales currently in use, thus managing to validate the app's tasks as a tool for assessing the deficit of fine movements of the hands and possibly as an adjunctive training tool for patients with cervical SCI.

Table 1. *Timetable of the development, use, and planned spread of the application*

Timing	Goal reached/to reach
September 2020 – September 2021	Application design and development
September 2021	Financing for application development (Nuvasive – Grant ID 1466)
October 2021	Approval of the application by the Ethics Committee of AUSL Romagna (prot. 8525/2021 - I. 5/233)
November 2021	Approval of the application by the Ethics Committee at the Montecatone Institute as "consecutive center"
December 2021	Application release (beta version) on the Apple Store
January 2022	Expected approval of the application by the Ethics Committees of Bologna and Ferrara
February 2022	Final version of the application after bug fixing
February 2022 – February 2023	Approximately 160 patients are expected to be enrolled (from the 4 centers involved in the study) to assess the impact of the app as an evaluation and training tool
August 2022	Preliminary data analysis
September 2022 – February 2023	Recruitment campaign of European centers available for the use of application
February 2023 – February 2024	Approximately 700 patients are expected to be enrolled (from the European centers that will join the study) to assess the impact of the app as an evaluation and training tool

Expected impact of the application on outcome

From the analysis of the data collected in the *study group*, it is expected to obtain first of all the confirmation of good integration of the application in the neurorehabilitative

scenario, with high percentages of compliance among patients in the use of the application through touchscreen devices[14]. In this sense it is believed that the familiar interface of these devices can determine not only an easy employment of them, but also a more intensive use of the application compared to the current evaluation scales and training exercises. Therefore, we expect to register more minutes per week of training in the *study group* compared to the *control group* with statistically significant values and a significant agreement in terms of Cohen k between the accuracy percentages and the execution times of the app tasks and the values recorded with GRASSP and 9-HPT in the *control group*. In relation to the greater training intensity, it is likely that there will be a faster trend of improvement both in GRASSP and in 9-HPT in patients who will use the app[15]. However, it is complex to predict the impact of the application in terms of functional and neurological outcome. From other studies[16] we learnt that app performance is affected by aging and specifically by age-related dexterity decline even in healthy patients. These results extend the knowledge that hand function and specifically dexterity declines with age, to app performance. In this field a similar trend is expected even with the use of SPINE FINE. The innovative tasks of the app and the use of the Apple Pencil should positively influence the parameters of the GRASSP and the 9-HPT registered at 18 months, but it is likely that a significant improvement in this sense will be noted even at 12 months, compared to the *control group*, as in other similar studies significant data emerged even after 6 months. The multifinger tasks are expected to have a greater impact on the functional outcome than on the neurological one, since some of them simulate gestures of common daily use, such as those to unscrew the cap of a bottle, to turn a knob to open a door, to adjust the knobs of home appliances for cooking or heating food / drinks, to turn a key in a lock and to grab small objects. We believe that this latter ability can have greater margins for recovery and improvement especially in those patients who will be able to perform tasks even with the Apple Pencil. From the comparative analysis it is expected to find higher performance indices at 6 and 18 months in the fine movements of the hands, with better values at muscle function grading especially at 18 months, among patients using the application compared to the controls. These expected data should also have a positive impact on the functional outcome indices with lower mRS values at 6 and 18 months in the *study group* and better reports over time also in terms of SWPS among the patients assessed and trained with the application. However, considering the strong influence of the walking autonomy in determining different mRS scores, from this point of view we do not believe to register significant differences between the *study group* and the *control group*, but only values marking a trend in favor of the use of the application.

Considering the intrinsic frailty of many cervical SCI patients, regardless of whether the application is used or not, it is expected that high ASA and CCI scores could negatively influence the functional outcome with statistically significant values. The testing duration with the application should be comparable to or slightly shorter than that typically needed for GRASSP, which require approximately fifteen minutes for each hand. In this sense, also thanks to the game-like interface of many tasks, an increase in stress is not expected in patients who will use the application, despite the doubling of the time necessary for the evaluation of their impairment of fine hand movements.

DISCUSSION

From the recent results reported in literature, it would emerge that, in the area of fine hand motility, a detailed post-operative classification of the deficit would allow for a more precise rehabilitation process. The advantage of using tools for the assessment of neurological deficit of the upper limbs in cervical SCI patients and the importance of being able to take advantage of tests performed through specific devices to integrate the assessment scales commonly used in clinical practice is already documented. Various devices have been developed in this sense, but all with relatively limited properties for upper limb assessment, often with user interfaces non-intuitive or truly uncomfortable for those patients on a wheelchair, and sometimes bulky to the point of forcing the patient to use them in spaces exclusively dedicated to neurorehabilitation. Many of these devices also have the disadvantage of restricting movement to a single joint. Given the complexity and fine motor control of prehension, this restriction to a small number of single joint motions fails to capture the full range of hand and wrist dysfunction, although constraining the complexity of movement simplifies and improves measurement capabilities. Moreover, for a correct use of these devices, complex specific calibrations are often necessary for customizing them for the patient's body size and for allowing their use both with the right and the left hand. This is the case of the ARMEO[13], of the MAHI Exo-II robotic device[3], of the devices ideated by Kamper et al.[17] and by Grasse et al.[8]. Differently from them, SPINE FINE provides the possibility of administering tests through touchscreen devices, widely used in daily life, portable, easily usable in any context and in multiple body positions, without constraining the joints of the upper limbs and not requiring calibrations or specific hardware adjustments for each patient. Compared to traditional assessment scales, SPINE FINE registers important additional information, not operator-dependent, “hand-targeted” and more reliable in terms

of functional outcome assessment, thanks to those tasks mimicking and evaluating some of the common gestures performed daily with the hands. The possibility of quantifying the correctness in the execution of tasks, the percentage of accuracy and the time taken to complete them, enriches the standard clinical evaluation with a specific tool for assessing multiple fine hand movements and with new quantitative and standardized data. Moreover, the portability and manageability of an iPad, through which the tasks of the application are administered, and the design of the tasks, almost in the form of a game, invite to train as well as to evaluate the fine movements of the hands, empowering the use of the application for longer periods even in places not specifically dedicated to neurorehabilitation. In fact, the patient, helped by the real-time feedback of the correct execution of each task, thanks to the color code of the error while tracing and to the final report produced, could autonomously self-assess the precision of execution in the various tasks administered and the time taken, experiencing the application more as a training tool that can be used even in full autonomy. In this sense application softwares on touchscreen devices together with robotic training with elements from virtual reality may be powerful tools to motivate patients to perform repetitive movements[13]. Motivation is essential for patients to be encouraged in therapy to attain short-term and long-term goals towards independence. Providing useful and enjoyable training can make it easier for patients to attain these goals. The increased time dedicated to exercises and the possibility of appreciating the progress in recovering fine movements of the hand through the simple report produced by the app and thanks to the accuracy percentage showed task-by-task, together with the color of the tracing, could lead to the development of a virtuous circle encouraging patients to dedicate more time to exercises for the hand motility. The patient's willingness to improve their skills with the hands could arise from the peculiarity of the application to be able to measure even small progresses in terms of percentages and seconds in performing the tasks, determining in the patient psychological reinforcement mechanisms and useful incentives to maximize the effectiveness of the neurorehabilitation program. Although similarly to other devices and applications, even SPINE FINE is not able to provide direct force and sensory measurements, it is believed that our application will demonstrate excellent reliability in recording quantitative data on finger, hand and wrist fine movements over time, which may be useful for long-term studies aimed at improving hand and wrist function after cervical SCI. The use of continuous physical values also largely mitigates any variance in tests that rely on a subjective scoring system, which would facilitate comparison of data across multiple sites in a trial. Moreover, unlike ordinal assessments, there is no performance ceiling or necessary stratification. The simple data stream collected with the application could also be easily implemented into a proper

video game architecture to increase engagement and promote user compliance. In this sense, the possibility of being able to design infinite tests aimed at investigating the possible compromission of any imaginable movement of the hands and fingers together with the advantage of being able to further implement and refine the application in the future, make SPINE FINE always updatable to the most recent standards of assessment and training and at the same time easy to improve and expand in its contents and interface. From research on the iOS and Android platforms and from the analysis of the literature, 3 applications with purposes similar to SPINE FINE were identified. Their preliminary results reported in rehabilitation after carpal tunnel surgery[18] or in general in patients in whom wrist, hand and/or fingers had sustained bone and soft tissue injuries that limited functional ability[19], as in the case of application ReHand, provide data for the quantitative evaluation of the accuracy of free movements of the fingers and wrist on the basis of dragging tasks to be performed within a predetermined time. Another application, KanDo, administers only tracing, steadiness, and reaction tasks, with the latter two scarcely useful in patients with cervical SCI. This application, while providing, as SPINE FINE, accuracy percentages and increasing levels of difficulty of the proposed tasks, binds, like ReHand, to the execution of tasks in predetermined times and it marks only few reference points for guiding patients to an ideal tracing. The third application, Dexteria, presents only tracing, pinching, and tapping tasks, but, while providing a report on the percentage of accuracy and the time taken to execute the various tasks as SPINE FINE, it only allows a tracing task of letters and numbers within spaces of tracking predefined by the app, without providing increasing levels of difficulty and forcing patient to start the task again in case of error. Therefore, the patient does not have immediate feedback on the degree of the tracing error as in SPINE FINE, but only numerical values in the final report, not allowing him/her to appreciate in real time the degree of the mistake made. In the pinching task is evaluated only the speed with which the patient succeeds in nipping *n* figures with increasing levels of difficulty. The task regards the presentation of a growing number of figures, even in movement, but assuming that the patient can correctly and quickly perform a pinching gesture. In the tapping task, on the other hand, virtual keys are proposed to be pressed with the second, third, fourth and fifth finger alternatively, according to a random presentation scheme, simulating tapping on a PC keyboard or on a piano. Recently used in individuals with mild-to-moderate upper-extremity impairment because of stroke, Dexteria, albeit in a limited number of patients, has shown utility in terms of training with better performance in the Box & Block Test (BBT), which is a test of manual dexterity[16]. Both Dexteria and KanDo have exclusively an English interface, with a task report that can be exported via email in Dexteria, and cannot be

exported in KanDo, with this latter showing graphics even difficult to be interpreted. ReHand, instead, allows a remote access to the task report through a shared account with the reference physician. In this sense both this application and SPINE FINE open the doors to the future design of the first telerehabilitation protocols. Compared to all the other apps that generally administer tasks with interfaces which allow to evaluate only the presence or absence of the correct hand movement/gesture to be performed, SPINE FINE allows to perform tasks, especially with tracing ones, with a wide range of graduality. In fact, the application is conceived to complete tasks even with gross tracing mismatches, quantifying these latters and without interrupting the task whenever an error occurs, as happens in Dexteria. In this sense, as noted by other authors[16], the possibility of proposing various levels of difficulty extends the use of the application to patients with more severe neurological deficits, providing precious parameters over time for an estimate of the impairment of the upper limb in a wider range of patients.

Limitations

The limitations of this study lie on the provided time of full operability of the application, related to possible bugs in the first weeks after its release and to the patients sample size necessary to validate SPINE FINE both as a tool for analyzing the impairment of the fine hand movements, and as a possible training tool. Other limitations are represented by the few studies in the literature on the use of tablets and applications as clinical evaluation and training tools and by the absence of studies on applications with these purposes, dedicated to patients with cervical SCI. The lack of precedents in this sense will require greater caution in the analysis of the data and a greater number of patients to support the results that will be obtained.

CONCLUSION

Based on the clinical evidence collected so far, we believe that the integration of the application into current clinical practice can provide additional, objective, quantitative and analyzable data, capable of enriching the current functional assessment of patients with cervical SCI. We estimate that the results of this study could lead to more targeted and effective rehabilitation programs. SPINE FINE could in fact determine better neurological

and functional outcomes *indirectly*, using the app as an integrative tool for evaluating patients with cervical SCI, thus allowing greater personalization of the neurorehabilitation path, thanks to the innovative data provided, and *directly*, using the app as a training tool. The evidence that will emerge from the study could therefore be of great impact if projected and applied in daily clinical management. In this sense, the publication of an extensive multicentric study would help to develop more effective and safe treatment algorithms in the context of a pathology that represents the most disabling spinal trauma in the population, especially in the most active from a social and work point of view. As dexterity especially in older adults has previously been found to be a strong predictor of functional independence and disability in basic activities of daily living and instrumental activities of daily living and daily arm-hand use, it is important to maintain good dexterity. Apps could possibly be used for training of dexterity with the few evidence on this field which need to be confirmed by future research.

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