Fashion or Need?

- Stroke
  - In the US
    - 795,000 strokes every year
    - Economic burden of $73.7 billion for 2010
    - 70% of the survivors need therapy
    - Total of 6 Million stroke survivors
  - In Europe
    - 900,000 strokes every year
  - In Japan
    - 200,000 strokes every year
  - In Brazil
    - Number #1 cause of death

Paradigm Shift in Neuroscience

- Myth and Legend:
  - Traditional care assumes that brain is hardwired and cannot recover once sensorimotor areas are destroyed

- Reality:
  - New understanding: after stroke and other neurological injuries plasticity occurs and might accounts for remapping of new pathways
Hardwired

- Since the 1928 work of Santiago Ramón y Cajal, famed neuroscientist, the prevailing assumption has been that the central nervous system is hardwired, non-malleable, and incapable of repairing itself.
- Clinicians have selected compensation as a rehabilitation strategy for non-remediable deficits of strength, voluntary motor control, sensation, and balance.


Paradigm Shift in Neuroscience

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Assistive, Prosthesis, Robotics

Paradigm shift

Barrow Sep 2016

% of population above 65 (UN 2006 Data Series)

- 1950
- 1960
- 1970
- 1980
- 1990
- 2000
- 2010
- 2020
- 2030
- 2040
- 2050

Western Europe
USA
Japan
India

Number of Publications

- 2014 Rehabilitation robots market at $454.3 million*
- 2020 Rehabilitation robots market expected to grow to $6.8 billion

Wintergreen Research; 2014-2018

Toyota
Honda
Yaskawa
Teijin
Hyundai
LG
Parker-Hannifin
Lockheed-Martin

Barrow Sep 2016
2010 Guidelines

Robot-assisted therapy offers the amount of motor practice needed to relearn motor skills with less therapist assistance. Most robots for motor rehabilitation not only allow for robot assistance in movement initiation and guidance but also provide accurate feedback; some robots additionally provide movement resistance. Most trials of robot-assisted motor rehabilitation concern the UE, with robots for the LE still in its infancy. Current robots tend to exercise only the proximal arm, and thus, they improve motor skills at the shoulder and elbow but not those of the unexercised wrist and hand; consequently, robots that only train the shoulder and elbow are limited in their ability to improve completion of ADLs.174 Robot-assisted UE therapy, however, can improve motor

---

2010 Guidelines

The U.S. Department of Veterans Affairs

Recommendations

1. Consider using treadmill training in conjunction with other task-specific practice and exercise training techniques in individuals with gait impairments and without known cardiac risk for treadmill exercise. [4]
2. Consider the use of partial body weight support for treadmill training (partial body weight support or total body weight support) in individuals with gait impairments and without known cardiac risk for treadmill exercise. [3]
3. Recommend using the standard anatomical position (SAP) for the patient with foot drop, to prevent foot drop and improve balance and stability during walking. [3]
4. Recommend using the anatomical position (AP) with the body in a supine position, specifically for patients with bilateral foot drop. [3]
5. Consider using a range of motion (ROM) and stretching exercises to improve self-care tasks of daily living. [3]
6. Consider using a range of motion (ROM) and stretching exercises to improve self-care tasks of daily living. [3]

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2010 Guidelines

The U.S. Department of Veterans Affairs

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6. Consider using a range of motion (ROM) and stretching exercises to improve self-care tasks of daily living. [3]
Is this true?

American Heart Association recommends Robot-assisted movement training and virtual reality for stroke rehabilitation
CSP558 – Veteran Affairs
Randomized Clinical Trial
CSP558: Robotic Assisted Upper-Limb Neurorehabilitation in Stroke Patients

Study Randomization Groups
- Robot-assisted Therapy (RT) – proximal or distal upper extremity segment movements and integrated whole arm movements
- Usual Care (UC) – customary VA chronic post-stroke care – includes an average of 3 therapy sessions per week of upper extremity training
  - Matching time in therapy
- Intensive Comparison Therapy (ICT) – a structured rehabilitative protocol that employs conventional techniques to match robot-assisted therapy in number of sessions, type, intensity, and quantity (“Charlie Chaplin Modern Times” therapy – Volpe et al., Neurorehab & Neural Repair, 22:3:305–310, 2008)
  - Matching time and intensity
- Active Treatment: 36 therapy sessions over 12 weeks.
- Evaluations: at 6, 12, 24 and 36 weeks
- RT better than UC by 5 points (MCID)
- RT better than ICT by 3 points (MCID – patients retain gains)
Study Population

• ≥ 18 years
• Moderate to severe upper extremity impairment
  - Fugl-Meyer score: 7 to 38
• Stroke occurring at least 6 months prior
• No upper limit on time since stroke
• Single Stroke
• Volunteers with multiple strokes were not excluded

Robots

- Consisted of 04 modules:
  - Shoulder-elbow
  - Antigravity
  - Wrist
  - Grasp-hand

Intensive Comparison Therapy
Baseline Entry Characteristics

- Age = 64.6 (±11.3) years
- 96% male
- 78% were white; 19% were black
- Ischemic stroke = 85%
- Time since index stroke = 4.7 years (0.5 to 23.6)
- Multiple strokes identified by imaging = 33%
- Fugl-Meyer Assessment = 18.9 (±9.5)
- Wolf Test times = 71.1 seconds (±33.2)
- Stroke Impact Scale = 49.4 (±14.7)
Primary Outcome – Fugl-Meyer Change at 12 weeks

- Comparison at 15 months when UC was dropped
- 24 months trial
- MCID 5 points
- Alternate MCID 3 points

<table>
<thead>
<tr>
<th>Overall Mean Difference over 12 weeks</th>
<th>Overall Mean Difference over 12 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fugl-Meyer Robot vs. UC = 2.17, p = 0.08</td>
<td>Robot vs. ICT = -0.14, p = 0.92</td>
</tr>
<tr>
<td>Wolf Robot vs. UC = -4.41sec, p = 0.22</td>
<td>Wolf Robot vs. ICT = 0.33sec, p = 0.82</td>
</tr>
<tr>
<td>MS Robot vs. UC = 7.54, p = 0.009</td>
<td>MS Robot vs. UC = 0.54, p = 0.81</td>
</tr>
</tbody>
</table>

Evaluations at week 12

Timeline and Evaluation

- Evaluations at 6, 12, 24, 36 weeks
- Their choice
- Usual care
- Intensive Matched
- Robot Group
- 6 months
- No therapy
- 24 months
Fugl-Meyer Change: 12 Weeks Intervention, Follow-Up at 36 Weeks

Comparison at 15 months when UC was dropped

24 months trial

Overall Mean Difference over 36 weeks
Fugl-Meyer Robot vs. UC = 2.88, p=.016
Wolf Robot vs. UC = -8.10sec, p=.005
SIS Robot vs. UC = 5.95, p=.04

Overall Mean Difference over 36 weeks
Robot vs. ICT = -0.58, p=.63
Wolf Robot vs. ICT = -2.13sec, p=.55
SIS Robot vs. UC = 1.19, p=.55

Cost for the VA Healthcare System
- Cost of 04 modules:
  - Shoulder-elbow
  - Antigravity
  - Wrist
  - Hand module
  - USD 230,750
Cost for the VA Healthcare System
Average per patient additional cost of therapy
• Robot Therapy U$5,152  p<0.001
• ICT U$7,382
• Usual Care U$0

Average total cost over 36 weeks (therapy + all other healthcare utilization)
• Robot U$17,831 (other healthcare $12,679)
• ICT U$19,746 (other healthcare $12,364)
• Usual Care U$19,098 (other healthcare $19,098)

Generalizability of CSP 558
• Outcome Assessments, mean (SD)
  • 200 individuals screened, 127 enrolled (64%)  
  • Time since index stroke = 4.7 years
  • Multiple strokes identified by imaging = 33%
  • Fugl-Meyer Assessment = 18.9 (±9.5)
  • Wolf Test times = 71.2 seconds (±33.2)
  • Stroke Impact Scale = 40.4 (±14.7)
• Constraint-Induced Movement Therapy
  • 3,626 individuals screened, 222 enrolled (6%)  
  • Fugl-Meyer 42.5 (11.7)
Sub-Acute (Inpatient)

- 1st study 10 inpatients (10 exp, 10 control)
- Experimental: at least 25 hours of interactive sensorimotor training
- Control: 5 hours of sensory training


- 2nd Study (30 exp, 26 controls)


Inpatients: Clinical Results

<table>
<thead>
<tr>
<th>Between Group Comparisons: Final Evaluation Minus Initial Evaluation</th>
<th>Robot Trained (N = 55)</th>
<th>Control (N = 41)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impairment Measures (± sem)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fugl Meyer shoulder/elbow (FM-se)</td>
<td>6.7 ± 1.0</td>
<td>4.5 ± 0.7</td>
<td>NS</td>
</tr>
<tr>
<td>Motor Power (MP)</td>
<td>4.1 ± 0.4</td>
<td>2.2 ± 0.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Motor Status shoulder/elbow (MS-se)</td>
<td>8.6 ± 0.8</td>
<td>3.8 ± 0.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Motor Status Wrist / Hand (MS/wh)</td>
<td>4.1 ± 1.1</td>
<td>2.6 ± 0.8</td>
<td>NS</td>
</tr>
<tr>
<td>Disability Evaluation</td>
<td>32.0 ± 5.0</td>
<td>25.3 ± 6.3</td>
<td>NS</td>
</tr>
</tbody>
</table>

Inpatients: Long-Term Benefits

"Is robot-aided sensorimotor training in stroke rehabilitation a realistic option?"; Volpe, Krebs, Hogan; *Current Opinion in Neurology* 2001, vol.14
Therapeutic Robotic Training: Inpatients

- Mass repetition: 20,480 point-to-point movements (4 week program)
- Impact of our Movement Therapy: experimental group improved 2 x control group (absolute scale: 10%)
- Recovery might continue far beyond 11 weeks post-stroke.
- The improved outcome was sustained after 3 years

Meta-Analysis of Robot-Therapy Trials on Motor Recovery

248 Stroke Patients
RATULS: Robot Assisted Training for the Upper Limb after Stroke

- NHS: National Health Service UK
- NICE: National Institute for Health and Clinical Excellence
- 4 hubs: Addenbrookes (Cambridge), Queens Hospital Romford (London), Western Infirmary (Glasgow) and North Tyneside Hospital North Shields (Newcastle)
- 16 hospitals
- 720 stroke patients
- Completion 2018

VA Multi-Site Trial

![Graph showing randomization data and baseline vs. 12 week Fugl-Meyer score difference]
Multitude of variables that may influence outcome, but little is known of the independence or interaction among these variables, nor their actual impact on outcomes.

Drive Neural Plasticity - Apply Motor Learning Principles

<table>
<thead>
<tr>
<th>Principle</th>
<th>Description</th>
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<tbody>
<tr>
<td>Use it or Lose it</td>
<td>Training that drives a specific brain function can lead to functional degradation.</td>
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<tr>
<td>Use it and Improve it</td>
<td>Training that drives a specific brain function can lead to enhancement of that function.</td>
</tr>
<tr>
<td>Specificity</td>
<td>The nature of the training experience dictates the nature of the plasticity.</td>
</tr>
<tr>
<td>Repeated Matters</td>
<td>Induction of plasticity requires sufficient repetition.</td>
</tr>
<tr>
<td>Frequency Matters</td>
<td>Induction of plasticity requires sufficient training intensity.</td>
</tr>
<tr>
<td>Time Matters</td>
<td>Different forms of plasticity occur at different times during training.</td>
</tr>
<tr>
<td>Schema Matters</td>
<td>The training experience must be sufficiently salient to induce plasticity.</td>
</tr>
<tr>
<td>Age Matters</td>
<td>Training-induced plasticity occurs more readily in younger brains.</td>
</tr>
<tr>
<td>Transference</td>
<td>Plasticity to response to one training experience can enhance the acquisition of similar behaviors.</td>
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<tr>
<td>Interference</td>
<td>Plasticity to response to one experience can interfere with the acquisition of other behaviors.</td>
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</table>

4. Repetition Matters
Induction of plasticity requires sufficient repetition.
Continuous Passive Motion Machine (sub-acute patients)

<table>
<thead>
<tr>
<th>Group</th>
<th>Pat</th>
<th>Time</th>
<th>MP</th>
<th>MSS/S,E</th>
<th>F-M/S,E</th>
<th>Joint stability</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPM</td>
<td>N=17</td>
<td>Adm</td>
<td>3.71±1.94</td>
<td>4.27±1.46</td>
<td>7.53±1.69</td>
<td>3.00±0.45</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Disch</td>
<td>9.70±1.3</td>
<td>9.20±1.3</td>
<td>10.90±1.1</td>
<td>2.4±0.4</td>
</tr>
<tr>
<td>Contr</td>
<td>N=15</td>
<td>Adm</td>
<td>1.33±1.00</td>
<td>1.22±0.49</td>
<td>5.20±0.49</td>
<td>3.53±1.94</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Disch</td>
<td>7.0±1.4</td>
<td>8.3±1.4</td>
<td>8.9±1.2</td>
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<td>Training that drives a specific function can lead to enhancement of that function.</td>
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<tr>
<td>9. Transfer</td>
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Passive vs Intention Driven Training Amount of Guidance in Unimpaired
Passive vs Intention Driven Training in Motor Habilitation

- Earth mean radius = 6,371 km
- Earth perimeter = 40,075 km
- 1 mile per day = 1.61 km
- 1 year = 1,834 km
- 66 years = 77,550 km
Distal Limb Segment

Learning, Not Adaptation, Characterizes CP Motor Habilitation: Evidence from Kinematic Changes Induced by Robot-Assisted Therapy in Trained and Untrained Task in the Same Workspace.

Admission                                      Discharge

Pii02                                        Pii03
Pii04                                        Pii05

(displacement in meters)
Training with Gravity Compensation vs. without Gravity Compensation

Spatial Training: Myth or Reality

Drive Neural Plasticity - Apply Motor Learning Principles

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Training Proximal vs. Distal Limb Segments

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</tr>
</thead>
<tbody>
<tr>
<td>190 outpatients (target 160 outpatients)</td>
</tr>
<tr>
<td>at Burke at NY Presbyterian at Unicampus</td>
</tr>
<tr>
<td>Group A: 6 weeks wrist + 6 weeks shoulder/elbow</td>
</tr>
<tr>
<td>Group B: 4 weeks shoulder/elbow + 4 weeks wrist</td>
</tr>
<tr>
<td>Group C: 12 weeks alternating days shoulder/elbow and wrist</td>
</tr>
<tr>
<td>Group D: 12 weeks same day shoulder/elbow and wrist</td>
</tr>
</tbody>
</table>

Barrow Sep 2016
### Changes per Site

<table>
<thead>
<tr>
<th>Site</th>
<th>Tableau de variance pour FM Disch-Adm</th>
<th>Graphique des interactions pour FM Disch-Adm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Campus Biomedico</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NY Presbyterian</td>
<td></td>
<td></td>
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### Training Proximal vs. Distal Limb Segments

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<tr>
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<th>Graphique des interactions pour FM Disch-Adm</th>
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<tbody>
<tr>
<td>alternate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>planar-wrist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>within</td>
<td></td>
<td></td>
</tr>
<tr>
<td>wrist-planar</td>
<td></td>
<td></td>
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</table>
Functionally-Based Rehabilitation: Benefit or Buzzword?

- Protocol – combined robot assist for transport with graded distal tasks involving actual objects.
- Hypothesis:
  - Specific, task-oriented training that combines robot assist with object grasp or manipulation would produce greater gains than “standard” robot training.

Breakfast with Tiffany’s
**Transition-to-Task**

- Impairment-based (A) vs. functionally-based (B)
- Which is best intervention for whom?
  - Motor Thresholds may indicate whether Rx A or B is most appropriate.
  - Continuum of intervention methods

---

**Functionally-Based Rehabilitation: Benefit or Buzzword?**

<table>
<thead>
<tr>
<th>Group</th>
<th>Transport of Arm (N=32)</th>
<th>Transport of Arm and Actual Grasp (N=10)</th>
<th>Transport of Arm and Virtual Grasp (N=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>25.0 ± 9.6</td>
<td>30.7 ± 16.3</td>
<td>21.4 ± 4.9</td>
</tr>
<tr>
<td>Group B</td>
<td>2.3 ± 2.5</td>
<td>2.1 ± 2.1</td>
<td>0.8 ± 2.5</td>
</tr>
<tr>
<td>Group C</td>
<td>1.7 ± 1.7</td>
<td>2.5 ± 2.5</td>
<td>0.2 ± 1.6</td>
</tr>
</tbody>
</table>

ANOVA p-value
- Between Groups: NS A vs B: p=0.20 A vs C: p=0.03

Functionally-Based Rehabilitation: Benefit or Buzzword?
Breaking It Down Is Better: Haptic Decomposition of Complex Movements Aids in Robot-Assisted Motor Learning

Nathan Klein, Member, IEEE, Steven A. Sprouse, Member, IEEE, and David J. Reinkemeyer, Member, IEEE

Functionally-Based Rehabilitation: Benefit or Buzzword?

Conclusion

Robotic training using a sophisticated exoskeleton improved behavioral outcomes of the affected upper extremity in chronic stroke survivors. Moreover, functional robotics training led to significant improvements in upper limb spasticity, challenge, and everyday activities. Successful completion of the robotic exoskeleton for more impaired subjects as well as providing a randomized controlled trial comparing this robotic training with conventional therapy to determine if BONES training is more effective than conventional therapy.
Unilateral versus bilateral robot-assisted rehabilitation on arm-trunk control and functions post stroke: a randomized controlled trial

The 3 groups did not differ significantly in the WHED, FMA, and ARAT scores (1400). However, significant differences were found in WHED Time (p=0.007, F=10.0, df=2, 975) Post has enhanced indicated that the URT group but not the CI or AT group showed lower WHED Time (p<0.01) than the BI group suggesting that significantly better movement efficiency occurred in the URT group than in the BI group.

The Effects of Combined Use of Robot-Assisted Therapy With Task-Specific or Impairment-Oriented Training on Motor Function and Quality of Life in Chronic Stroke

Continuum of intervention methods

Transition-to-Task

- Impairment-based (A) vs. functionally-based (B)
- Which is best intervention for whom?
  - Motor Thresholds may indicate whether Rx A or B is most appropriate.
  - Continuum of intervention methods
UE Robotic Therapy: Efficiency?

- Assessing a rehabilitation technique:
  - whether gains are as good or better than other modalities
  - whether gains persist for a significant period after training
  - whether gains generalize to untrained tasks
  - Whether cost/benefit are as good or better than other modalities

---

**RATULS Newsletter**

You can see improvements in my score, I don’t even mind doing the circles anymore, I think even with resistance I would push on through.

Wendy will say knuckles up or knuckles down, I have my eye on the leader board crown, I think my arm is getting stronger, I can do the exercises longer.

---

**Robotics in Stroke Rehab**

Thank you
hikrebs@mit.edu