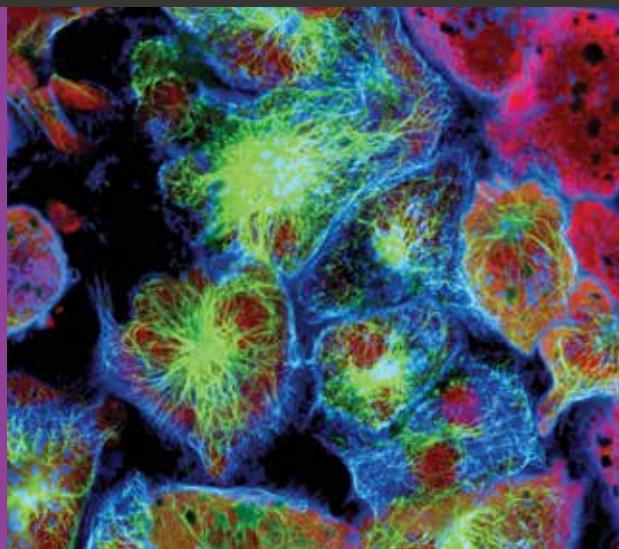




**CREATING THE FUTURE
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"WE HAVE
WHAT
EVERYBODY
WANTS"

"WE HAVE WHAT EVERYBODY WANTS"

A trusted colleague and mentor imparted this piece of wisdom to me as I was taking over as chair of the department last year. I think this idea is the sum of many parts, all adding up to how we as physiatrists, and we as a department, are primed to effect great change during a time of great uncertainty in medicine.

Physiatrists have an opportunity to be leaders in the changes taking place around us in all aspects of health care. As the concepts of interdisciplinary team work, patient-centric care, and a focus on preserving, protecting, and restoring function are rapidly integrating into all of medicine, we understand and realize that these themes are what we have always done, and done well, as rehabilitation medicine specialists. These are not new ideas. They are the core of our discipline. As such, we are primed to thrive in this new, evolving landscape, and our expertise will also allow us to help other disciplines improve the quality of care they provide and the value they contribute in unprecedented ways. It's a matter of our stepping up and seizing the opportunity to create and lead these new models of care.

Our department is undergoing a significant period of growth and expansion in virtually every existing area and many new ones. We are adding faculty and staff to support our increasing capacity for clinical care. It's something most programs strive toward, however, in these uncertain times, not all are able to achieve. We continue to develop new educational initiatives, conduct and promote groundbreaking research, and expand in both our inpatient and outpatient environments.



Developing new models of care in settings we've not traditionally been a part of is another reason for our growth, some of which is illustrated in this year's report.

Not only is this a testament to our talented faculty and staff, it is the crystallization of the thoughts and plans that our organization has to meet these challenges head on. UPMC leadership sees, understands, and supports our ability to influence and implement changes across our entire health system that will improve the lives of those in our care.

With all this in mind, I am pleased and honored to share with you this year's Highlights Report for the UPMC Rehabilitation Institute and Department of Physical Medicine and Rehabilitation. This by no means is an exhaustive list of our ongoing endeavors, but it does showcase the range of the research and clinical care programs conducted by our dedicated researchers, clinicians, and support staff. I have no doubt that these teams and individuals, alongside the rest of our department, will indeed thrive and lead us in the pursuit of the medicine of tomorrow.

Gwendolyn Sowa, MD, PhD

A handwritten signature in black ink, appearing to read "G. Sowa".

Director, UPMC Rehabilitation Institute
Chair, Department of Physical Medicine and Rehabilitation



BODIES IN MOTION:
*EARLY MOBILITY
AND REHABILITATION
IN THE ICU*

The idea that motion, or physical activity, imparts beneficial effects on an individual is not new. The scientific literature is vast on this topic, on everything from cardiovascular health, to brain aging and cognitive decline, to tissue healing. Motion, movement, activity, it may be said, is a fundamental characteristic of being alive.

When it stops or significantly slows — either voluntarily or involuntarily — a host of health issues may arise and lead to a cascading effect of bad outcomes and poorer overall health. For patients who end up in the intensive care unit (ICU) as a result of illness, injury, transplant, or trauma, there is a growing interest and trend in getting them mobilized as early as possible, and involved in degrees of rehabilitation to aid them in their recovery process to avoid or mitigate possible complications associated with prolonged rest or physical inactivity.

Within the UPMC Rehabilitation Institute, Julie Lanphere, DO, assistant professor and medical director of inpatient rehabilitation at UPMC Montefiore, is spearheading several new early mobility initiatives for both ICU patients and non-ICU patients throughout the broader UPMC health care system. Dr. Lanphere is part of the ICU service line task force, and she is leading the mobility initiative to make this type of care routine in the ICU through the development of consistencies and standards of care across the entire system. Her ultimate goal is to make early mobility a part of routine care, not just for ICU patients but for all patients admitted to the hospital.

"In the end, I want to see patient mobility assessed as a vital sign, a component of patient care that we as practitioners evaluate every single day a patient is in our care, no matter what level of care they are at in the hospital. My expectation is that we will make that happen in time," says Dr. Lanphere.

THE BENEFITS OF EARLY MOBILITY

ICU patients who are on prolonged bed rest, and those who also are under sedation for long periods, are susceptible to numerous complications. These include loss of muscle mass, neuromuscular system degradation, ventilator-associated pneumonia, deep vein thrombosis, ICU-acquired weakness or critical illness myopathy, delirium, cognitive impairments, and psychological distress. Any of these complications are problematic for critically ill individuals and, when combined, lead to longer, more difficult recovery trajectories and increased morbidity and mortality.

"We know there are a number of consequences to prolonged bed rest or immobility, and with the subset of patients that are under sedation for extended periods of time due to their illness

or injury, those consequences are sometimes magnified and more difficult to manage," says Dr. Lanphere. While these complications are serious, some even life-threatening, they can be addressed or mitigated, and early mobility is an intervention that works.

Dr. Lanphere's initiative in the ICU at UPMC Montefiore has the objective of mobilizing patients within 24 to 72 hours after admission. This objective, of course, takes into account each patient's specific condition and needs. And it can only be done by working in close collaboration with the ICU physicians, nursing staff, and physical therapists to assess and make plans for each patient to get them up and moving to the degree which they are capable.

Not all patients are immediate candidates for early mobility and rehabilitation. Individuals with acute respiratory distress syndrome, those with a pulmonary embolus with accompanying cardiac risks, head injuries, and others may need to stabilize further before attempting any mobility tasks.

"There are definite safety parameters we follow when assessing patients and introducing mobility into their care, and this can change from one moment to the next, which is why our assessments and interventions are not static. They change as the patient's condition changes," states Dr. Lanphere.

Mobility and rehabilitation for ICU patients can take many forms, not just walking across the room or down the hall. It may include breaks in a patient's sedation, sitting them up in bed, range of motion exercises that are either passive or active depending on the patient, or even just talking to them and getting them to interact verbally with their caregivers. For critically ill patients, sometimes just orienting them to time and space, particularly those coming out of sedation, can be of significant benefit.



TOP 10 REASONS FOR EARLY MOBILITY

In August 2016, Dr. Lanphere co-authored a paper in the journal *Intensive Care Medicine* titled "Ten Reasons Why ICU Patients Should Be Mobilized Early." Along with her colleagues Dale Needham, MD, PhD, of Johns Hopkins, and Linda Denehy, PhD, of the University of Melbourne, they present a detailed case for early ICU mobility. The paper makes plain the benefits to patients along numerous avenues, addresses concerns about patient safety and possible barriers to implementation, outlines

the current evidence base on early mobility, and advocates for more research on multiple fronts to expand this evidence base.

"Nationwide, we are trying to push towards routine care. This should not be a program for specific patients; this should be a program for all patients. This should be a routine standard of care for all patients," says Dr. Lanphere.



“Early mobility should not be a program for specific patients. It should be a standard of care for all patients.”

EARLY MOBILITY AND DELIRIUM

Delirium is of major concern for all ICU patients. For patients on a ventilator, the incidence of delirium approaches 80 percent. The effects of delirium are well documented and costly in terms of mortality, length of stay, and possible post-delirium cognitive impairments and emotional distress. ICU early mobility has the ability to dampen such symptoms and lessen their incidence.

Dr. Lanphere is involved in several initiatives within UPMC to tackle the problem of delirium in the ICU through mobility, and she is part of the task force with the Society of Critical Care Medicine currently working on updating the Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit. Last updated in 2013, Dr. Lanphere and her colleagues have been at work for more than two years, reviewing the literature and working to update the guidelines to include the role of mobility, which will be introduced for the first time.

Mobilization is also part of the guidelines of care used across UPMC to assess and treat delirium in the ICU, and Dr. Lanphere is responsible for helping to develop these guidelines and advocate for their use. For patients under sedation, breaks in that sedation and mobilizing them can often give clues or show telltale signs that a patient is experiencing delirium or having adverse psychological reactions to their medications and bed rest. In this way, mobility can be a kind of diagnostic tool and allow clinicians the ability to intervene. Things such as pain and agitation can also be uncovered and addressed.

“We are approaching this in a multidisciplinary fashion. The doctors and nurses in the ICU, along with rehabilitation, all need to be on the same page with how sedation practices are handled, and how we look for and treat delirium.”

RESEARCH WILL DRIVE ACCEPTANCE AND IMPLEMENTATION

On some level, it ought to be intuitive to accept the benefits of early mobility for ICU patients and work to implement such interventions where appropriate. Of course, intuition is not the same as good science backed up by a body of evidence and confirmed through trial and replication of results. What the realm of early mobility in the ICU currently lacks is a large evidence-base to give the concept broad support.

This is largely due to the fact that the entire concept is virtually new. That will, in time change, Dr. Lanphere indicates, as more trials are conducted and the broader cultural, operational, and patient safety hurdles or barriers to implementation are addressed, again through trial and with evidence to support mobility interventions for this patient population.



Quality improvement initiatives at UPMC under the direction of Dr. Lanphere have been able to show feasibility. This is the first question that has to be addressed: How feasible is it to mobilize ICU patients? For example, can a patient on a ventilator be mobilized in any way? And how safe is it to do so for the individual?

"We've shown feasibility with several quality improvement projects, and we've also shown that it can be done safely by following standards of care and through close collaboration," says Dr. Lanphere.

Outside of the ICU, Dr. Lanphere has pursued mobility quality improvement research in the acute hospital patient population by comparing patient and nurse cohorts using activity trackers to log their activity with stated goals against baseline data. Baseline data was derived by giving a cohort of patients activity tracking devices without telling them what the device was for or why they were to wear it.

Subsequent phases of the trial gave specific and measurable goals to the patients and nursing staff related to the number of steps they were to try and achieve each day during their stay. Patients were informed each night of their progress and encouraged to continue to reach or exceed their goals.

"Patients and nursing staff absolutely loved it. The patients felt like they had some accountability for their care and were able to participate in their own care," says Dr. Lanphere.

Other initiatives throughout UPMC are under the leadership and direction of several mobility champions, including nursing staff getting patients up for meals three times daily to improve the mobility culture and working to prevent aspiration and improve cognition and patient engagement. It's a tremendous effort by all to change to a mobility culture.

MULTIDISCIPLINARY AND COLLABORATIVE

Rehabilitation medicine is an inherently collaborative discipline. And by its very nature, the early mobility initiative under Dr. Lanphere's leadership is, and must be, a partnership between everyone involved. ICU physicians and nursing staff, patient care managers, rehabilitation therapy team members, all the way up to hospital administration must all engage and collaborate with one another for success. No two ICU patients are the same. Each must be assessed for readiness for mobility interventions — what types of interventions are possible given the patient's status and needs — and actively monitored and reassessed as his or her time in the ICU progresses. The medical fragility of these patients can change quickly and unexpectedly; however, with close supervision, collaboration, and defined standards of care, critically ill ICU patients can be given a head start on their road to recovery.

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The Center for Spinal Cord Injury at the UPMC Rehabilitation Institute, and the University of Pittsburgh Model Center on Spinal Cord Injury (UPMC-SCI) continue as a national leader in clinical care and research for patients with spinal cord injuries (SCI), be it through trauma or disease.

SPINAL CORD INJURY AT UPMC:

*A MODEL SYSTEM
FOR RESEARCH AND
CLINICAL CARE*

Clinical care is led by Amanda Harrington, MD, director of Spinal Cord Injury Services at the UPMC Rehabilitation Institute, while the Model Systems grant is led by co-directors Michael Boninger, MD, and Lynn Worobey, PhD, DPT. Drs. Harrington, Boninger, and Worobey, along with their colleagues from both clinical and research programs, are working to transform and improve the nature of acute care, post-injury rehabilitation, and the long-term function and quality of life for patients with spinal cord injury.



EXCELLENCE IN RESEARCH: UNIVERSITY OF PITTSBURGH MODEL CENTER ON SPINAL CORD INJURY

One of only 14 such centers in the United States, the University of Pittsburgh Model Center on Spinal Cord Injury received funding in 2016 from the National Institute on Disability, Independent Living, and Rehabilitation Research (NIDILRR) for another five-year cycle. Renewed funding will allow investigators to continue their SCI research, as well as recruit patients into the SCI National Database, the largest database of its kind longitudinally tracking SCI patients for up to 40 years after their initial injury.

The program has been a model system for the last 15 years, during which time it has collaborated with other model system institutions and spearheaded its own research projects. While research projects and involvement have changed over the years, Dr. Boninger and his colleagues' model system's research focuses on teaching individuals two important skills related to their spinal cord injury. "People with SCI need to know how to transfer in and out of their wheelchair. They also need to know how to maintain their wheelchair in order to keep it from breaking down," says Dr. Boninger.

Teaching Transfer Skills and Measuring Outcomes

Dr. Worobey explains that during the last cycle of grant support that ended in 2016, research¹ was devoted to understanding the impact of transfers on the development of injuries or associated pain. "Transfers are an essential mobility skill, and a gateway to independence and quality of life. Because they are done with high repetition, we looked at the biomechanics of how someone transfers to identify optimal techniques. From there, we developed an in-person training program to teach or improve biomechanical techniques as a way to reduce or prevent injuries and pain," says Dr. Worobey.

What also came out of this research was the development of an outcome measure for assessing transfers, a tool that previously did not exist. This research is helping doctors to better understand the nature of secondary complications associated with transfers and the new demands they place on individuals with spinal cord injuries, and to provide practical interventions to improve quality of life for patients.

As part of the new cycle of grant funding, Drs. Boninger, Worobey, and colleagues will continue their research into transfers by developing a web-based training program designed to teach and improve transfer skills that are normally taught in person. In addition, "In a systematic way we will evaluate whether this training is able to change people's behavior or impact their daily lives in a positive way," says Dr. Boninger. Web-based training materials also will be developed for clinicians to assist with their in-person education efforts.



These efforts will be multidimensional and will attempt to address certain challenges that are known about web-based learning for this patient population. "We plan to enroll patients nationally in our randomized controlled trial, but we will need to develop ways to create awareness and work around the fact that approximately 30 percent of people with spinal cord injuries do not have access to the Internet," says Dr. Worobey. This will entail several measures that look at community engagement tactics to support the dissemination of the training program. In terms of the actual training materials, Dr. Worobey explains that a unique part of the research will involve a social media group in which individuals can interact with one another to share their experiences. Content experts from UPMC-SCI will interact and serve as moderators for the forum to ensure the information is accurate and reputable.

Interventions to Curb the Incidence of Wheelchair Failures

Recent research by the UPMC-SCI team indicates that 62 percent of wheelchair users experience a wheelchair failure in a six-month period.² This is a significant problem for individuals with SCI, as the effects of a device failure can ripple across all aspects of their lives. Unfortunately, only a small percentage of wheelchair users are engaged in their own maintenance efforts. A collaborative research project³ led by Drs. Worobey and Boninger during the last cycle was designed to see whether group training in skills and maintenance for wheelchair users could improve outcomes.

"Our new research project builds upon the work of our group training efforts.⁴ We will take the content developed for those classes and move it into another web-based training portal. Teaching people how to change tires or preventatively clean their casters may go a long way to maintaining mobility and quality of life, before some type of mechanical failure occurs," says Dr. Worobey. Along with basic skills training, the research team is planning to develop a smart phone application in collaboration with Brad Dicianno, MD, associate professor, medical director of the UPMC Center of Assistive Technology, and director of the UPMC Adult Spina Bifida Clinic. Individuals can report, in real time, what's failing on their wheelchair, what the consequences are, and how their wheelchair dealer is responding to address the problem. This project will leverage past work and experience by Dr. Dicianno and colleagues who have developed a mobile application, the Interactive Health and Rehabilitation (iMHere) platform⁵ designed to support individuals managing chronic disabilities.

Drs. Worobey and Boninger are excited to continue their research as a Model System entity. These efforts may bring to light new findings and adaptations to the training content. "We are building two very different interventions, and it will be interesting to see how effective they are. We may find that motor skills learning doesn't work as well in a web-based setting but basic maintenance skills do. And, of course, as we learn what does or does not work, we'll adapt to better meet the needs of individuals with spinal cord injuries," says Dr. Worobey.



Wheelchair Skills Training Improves Quality of Life

Clinicians in the Spinal Cord Injury Program know that many wheelchair users lack critical skills to access the community, like wheelies, or negotiating curbs and uneven terrain, and transferring in and out of the chair. These skills are closely tied to quality of life and participation in activities of daily living.

Through the work in the Collaboration on Mobility Training (COMIT) multisite study of wheelchair skills and maintenance (led by the UPMC-SCI), it was demonstrated that group classes on developing wheelchair skills and maintenance abilities have a positive effect on participants. Using the findings of the study as a launching point, Dr. Worobey and her colleagues developed a program to integrate these classes into the clinical care of the Spinal Cord Injury Program at UPMC.

The classes, led by Dr. Worobey and colleagues from the UPMC Centers for Rehab Services, are open to current patients on the rehabilitation units, as well as to wheelchair users in the community. Classes are held once a month for 90 minutes and cover a range of topics and hands-on skills training for individuals based on their personal goals. "We use a goal attainment scale for participants to set individualized goals and rank their confidence with different wheelchair skills," says Dr. Worobey.

Programs such as the wheelchair skills clinic are a direct example of how the researchers and clinicians in the UPMC-SCI are translating their research from the Model System program into evidence-based interventions to improve the lives of their patients and members of the community at large.



CLINICAL CARE FOR SPINAL CORD INJURIES



For Amanda Harrington, MD, the focus of the UPMC Rehabilitation Institute Center for Spinal Cord Injury has always been, and will continue to be, a focus on providing excellence in

clinical care for individuals with spinal cord injuries. Be it through quality improvement measures, education and training programs for staff and patients, or expanding the scope of care to new patient populations, there remains a focus on preserving and optimizing function, and the difficult task of helping individuals adapt to a new world with new challenges.

The 20-bed inpatient unit located within UPMC Mercy treats a diverse mix of patients with traumatic injuries, or nontraumatic causes stemming from spinal cord strokes, infections, and conditions such as multiple sclerosis, as well as a subset of oncology patients. The comprehensive team of physicians, therapists, nurses, and neuropsychologists are coupled with case management and nutrition services to provide medical and rehabilitation support to persons with new spinal cord injuries, and to assist with reentry into the community.

Evolving Care Through Clinical Research and Quality Improvement Initiatives

Staff members within the Center for Spinal Cord Injury are actively involved in ongoing research and clinical quality improvement

initiatives. Interdisciplinary teams attend and present at national meetings for professionals working in spinal cord injury rehabilitation.

Recent presentations by members of the team have focused on the management of older patients with central cord injuries and the management of oncology patients with SCI. Presently, one of the UPMC SCI physical therapists, Joseph Everhart, DPT, is working on a quality improvement project to evaluate the use of predictive models to help plan a rehabilitation program to better fit each individual patient with an incomplete injury. "If we can better predict who might be able to walk after their injury, and plan their treatment course accordingly, we can improve the clinical management of these patients with incomplete injuries," says Dr. Harrington.

Psychological Support for Patients

People with spinal cord injuries almost universally have some adjustment to their new disability. Dr. Harrington indicates that many patients participating in spinal cord injury rehabilitation have psychological needs that must be addressed. "We have two neuropsychology faculty members working on the spinal cord injury unit. Every patient who is admitted to our unit, as part of their routine clinical care, is evaluated and supported by our psychologists. They are an integral part of our team, which is not always the case with other programs," says Dr. Harrington.

Educational Initiatives for Patients and Providers

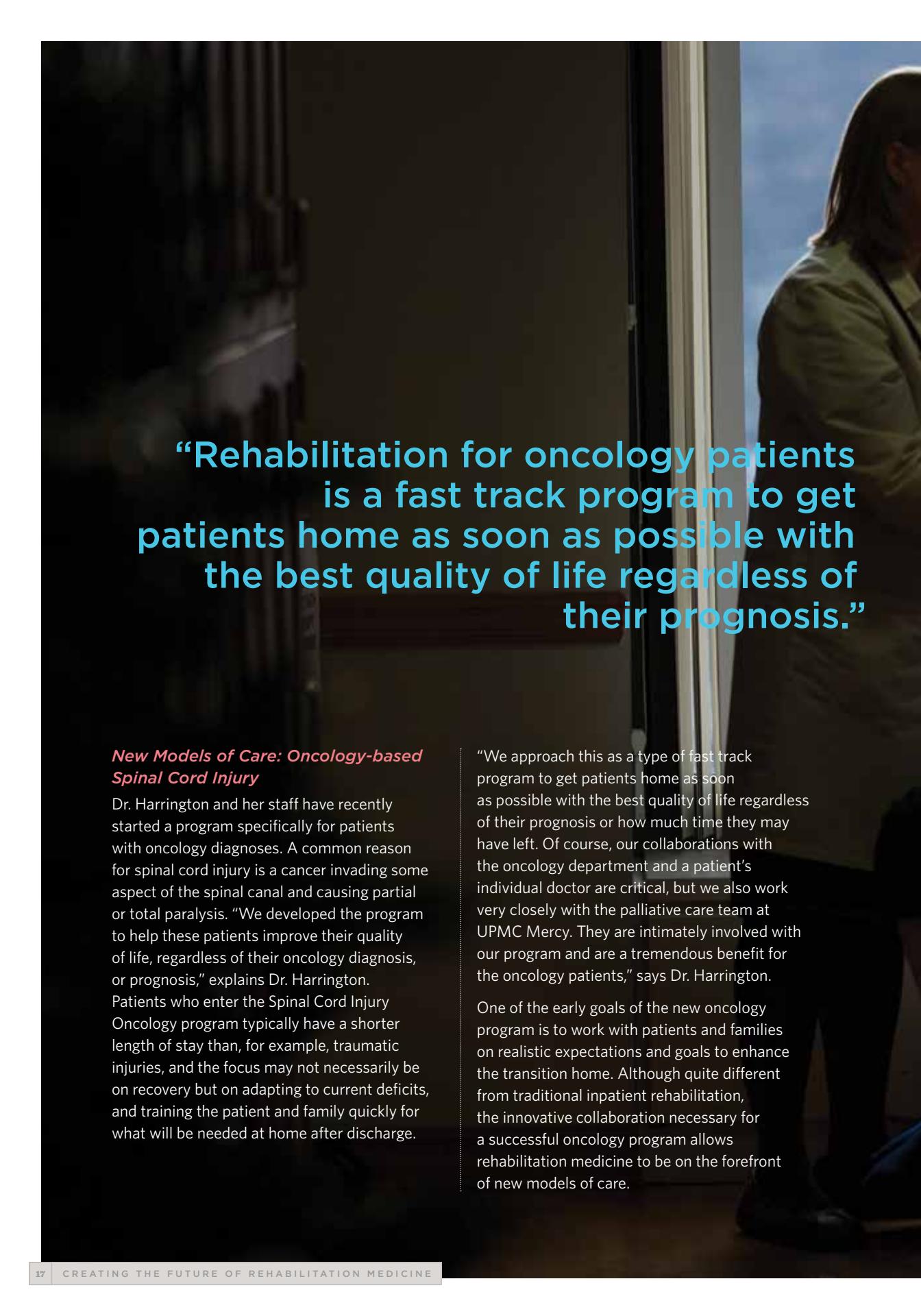
For people with newly acquired spinal cord injuries, all aspects of their daily lives are affected. A large component of their inpatient rehabilitation is focused on education and training to learn or relearn skills, adaptive strategies, and ways to deal with the medical complications they may encounter after discharge.



New patients on the unit take part in one-hour education sessions three days a week in a group setting. The comprehensive sessions are taught by the nutrition, physician, therapy, psychology, and case management staff, all discussing different topics of relevance to people with newly acquired injuries. "Education sessions, which occur in a group setting in the dining room, are an integral part of our program. We touch upon medical and rehabilitation topics, discharge planning, adjustment concerns — the real basics pertaining to all the new changes people are dealing with and trying to adapt to early on in their care," says Dr. Harrington.

For providers caring for spinal cord injury patients, Dr. Harrington and her colleagues coordinate and host an annual conference called *Current Concepts in Spinal Cord Injury*

Rehabilitation. Started in April 2015, this local educational event is open to providers and caregivers from any health care institution who are interested in learning from some of the nation's leading experts in the comprehensive care of spinal cord injuries. "We bring together therapists, nurses, physicians, and anyone interested in spinal cord injury to share our experience, knowledge, and recommendations for treating these complex injuries," indicates Dr. Harrington. The 3rd Annual Current Concepts in Spinal Cord Injury Rehabilitation conference is scheduled for April 29, 2017 at UPMC Mercy in Pittsburgh, Pennsylvania. The conference has a number of hands-on breakout sessions geared to therapists, nurses, and physicians with both basic and advanced experience in working with individuals with spinal cord injuries.



“Rehabilitation for oncology patients is a fast track program to get patients home as soon as possible with the best quality of life regardless of their prognosis.”

New Models of Care: Oncology-based Spinal Cord Injury

Dr. Harrington and her staff have recently started a program specifically for patients with oncology diagnoses. A common reason for spinal cord injury is a cancer invading some aspect of the spinal canal and causing partial or total paralysis. “We developed the program to help these patients improve their quality of life, regardless of their oncology diagnosis, or prognosis,” explains Dr. Harrington.

Patients who enter the Spinal Cord Injury Oncology program typically have a shorter length of stay than, for example, traumatic injuries, and the focus may not necessarily be on recovery but on adapting to current deficits, and training the patient and family quickly for what will be needed at home after discharge.

“We approach this as a type of fast track program to get patients home as soon as possible with the best quality of life regardless of their prognosis or how much time they may have left. Of course, our collaborations with the oncology department and a patient’s individual doctor are critical, but we also work very closely with the palliative care team at UPMC Mercy. They are intimately involved with our program and are a tremendous benefit for the oncology patients,” says Dr. Harrington.

One of the early goals of the new oncology program is to work with patients and families on realistic expectations and goals to enhance the transition home. Although quite different from traditional inpatient rehabilitation, the innovative collaboration necessary for a successful oncology program allows rehabilitation medicine to be on the forefront of new models of care.



REFERENCES AND READING RESOURCES

The references below correspond to citations in this text and are only a selection from the full body of work completed to date by the UPMC-SCI. For a more complete listing of publications related to the recent work of the UPMC-SCI, please visit UPMC-SCI.Pitt.edu.

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A SENSE OF TOUCH IN NEURAL PROSTHETICS RESEARCH

Neural prosthetics, or brain-computer interface (BCI), research at UPMC and the University of Pittsburgh has, over the course of the last several years, significantly advanced the field with several firsts. The latest occurred in October 2016, when the multidisciplinary research team led by Jennifer Collinger, PhD, and Robert Gaunt, PhD, along with colleagues Michael Boninger, MD, Andrew Schwartz, PhD, and Elizabeth Tyler-Kabara, MD, demonstrated the ability of electrical stimulation within the somatosensory part of the brain to provide tactile sensations in aspects of the hand and fingers in an individual with a spinal cord injury.



Jennifer Collinger and Robert Gaunt

Past research² by the team has demonstrated the ability of an individual to control a robotic prosthetic arm with their thoughts, using neural signals decoded from implanted microelectrode arrays in the motor cortex. Subsequent research published in 2015³ expanded upon that work, and for the first time demonstrated arm movement with 10 degrees of freedom. Essentially, 10 degrees of freedom of movement means that the individual was able to move the arm around, control the wrist, and also move the thumb and fingers in relation to space and with objects. The fingers cannot all be moved independently, but much of the normal capabilities of the hand are possible.

SENSATION IS KEY TO MORE NATURAL CONTROL OF NEURAL PROSTHETICS

Sensation is a critical element to movement and, in particular, interaction or manipulation of objects. The past studies have shown that participants could learn to use and manipulate a robotic arm through thought-provoked decoding of neural activity from the motor cortex. What was missing was the addition of feeling or sensation during interaction with objects.

Now, in a study¹ published in October 2016 in *Science Translational Medicine*, the research team has shown the ability to realize partial sensation in the hand of an individual with a spinal cord injury.

For this study, the participant, Nathan Copeland, who suffered a spinal cord injury in an automobile accident 10-years prior, had two tiny (2 mm x 4 mm) microelectrode arrays implanted directly into regions of the somatosensory cortex associated with sensing touch from his right hand and fingers, along with another set of microelectrodes implanted in the motor cortex to control aspects of motion.

Placement of the microelectrode arrays during surgery, conducted by neurosurgeon Dr. Tyler-Kabara, were guided by preoperative functional and structural magnetic resonance imaging, as well as magnetoencephalography (MEG) to ensure optimal placement of the arrays to facilitate both the necessary motor control and anticipated sensory stimulation of aspects of the right hand. (See Figure 1A-C in Flesher, et al.¹ for detailed descriptions of array placement and mappings to areas of the hand.)

The implant surgery for this study occurred in May 2015. The participant adapted to controlling the robotic arm fairly well from the beginning, following a defined training paradigm and control strategies used with the first study individual. "There was a little bit of learning with Nathan in terms of getting better and more consistent control with performance, but he adapted in a similar fashion as our previous study participant," indicates Dr. Collinger.

As Dr. Gaunt explains, expectations for the study were that the implants would generate some sensations and that the patient would be able to describe them. "Nobody had ever done this before, so there were a lot of new things to figure out. However, fairly early on in the study, within the first four weeks, we were able to show conclusively that in our patient the microstimulation produced the

ability to feel sensations, where they occurred in the hand, and basically how they felt," says Dr. Gaunt.

NEW LEARNINGS AND UNEXPECTED FINDINGS

The aspects of Nathan's hand that he has sensation in (the base of the fingers) are slightly different than what was hoped for with the placement of the microelectrode arrays. This has necessitated some changes in the way the team thinks about some of the experiments with Nathan, because they cannot generate sensations that feel as though they are coming from the tips of the fingers. But at the same time, this is also giving the researchers opportunities to design new experiments to see whether they really are limited to the stimulated regions that are in place now or if there is the potential to manipulate them. It's a challenge and an opportunity as Dr. Gaunt explains.



Former study participant Jan Scheuermann.



Andy Schwartz (l) and Robert Gaunt (r) with members of the research team and study participant Nathan Copeland.

ARTICULATING THE EXPERIENCE

Collecting the patient participant's descriptions of the sensations was one of the primary reasons for the experiments. While the research has a structured way to go about collecting this information, obtaining the information proved to be more difficult than anticipated. Dr. Collinger explains that while Nathan is able to express where the sensations are occurring, and with what intensity or if they feel natural, obtaining more detailed descriptions has been challenging, because the sensation that he has is not necessarily the same kind of experience that he had before his accident.

For Dr. Boninger, the quantification of sensation by the participant is both interesting and a recognized challenge of the study. "One of the founders of the study, DARPA, has devoted resources to try to make sure that there are tools available that can measure our ability to restore sensation and its impact on function. This is such a new area of study that part of what you need is new tools to measure such things. Part of the reason it might be difficult for Nathan to describe what's happening is that this is a totally new experience. One could argue that's a detractor from the experiment, but I think the reality is that's how the human body perceives things, and

those perceptions can change over time. The whole sensory and motor learning component of our studies — we're just starting to scratch the surface."

ONGOING RESEARCH

Drs. Collinger and Gaunt and the rest of the study team are progressing in their research with BCI technology and continue to work with Nathan. For Dr. Gaunt, the research is moving into trying to show that sensory feedback can improve the ability of the subject to control and manipulate the robotic arm. "That's really our goal: better, more natural functional control of the prosthetic. We are discovering that there are actually many components to that, and how that sensory information is transmitted to the nervous system is a focus of mine," says Dr. Gaunt.

For Dr. Collinger, whose primary focus area of the study is with motor control, the common goal of the continuing research is to see how sensory feedback can improve motor control. "Now that we've demonstrated sensory feedback, we can try to improve our control scheme of the robotic arm to do a number of things, such as regulating the amount of force applied when manipulating an object."

A photograph showing several surgeons in blue surgical gowns, caps, and masks working on a patient's hand. The patient's hand is visible in the center, surrounded by medical instruments and equipment. The surgeon on the right is wearing a blue surgical mask and has a blue earring. The background shows a typical operating room environment.

Dr. Tyler-Kabara in surgery.

“Within the first four weeks, we were able to show conclusively that in our patient the microstimulation produced the ability to feel sensations, where they occurred in the hand, and basically how they felt.”

SMALL, INCREMENTAL STEPS WILL LEAD TO SIGNIFICANT BREAKTHROUGHS

The significance of the team's accomplishment was highlighted when members of the research team and the study participant, Nathan Copeland, demonstrated the technology and their progress to President Barack Obama during his visit to Pittsburgh for the White House Frontiers Conference on October 13, 2016. Mr. Obama shook the robotic hand controlled by Nathan while addressing the importance of this type of research and the advances being made by dedicated researchers and participants.

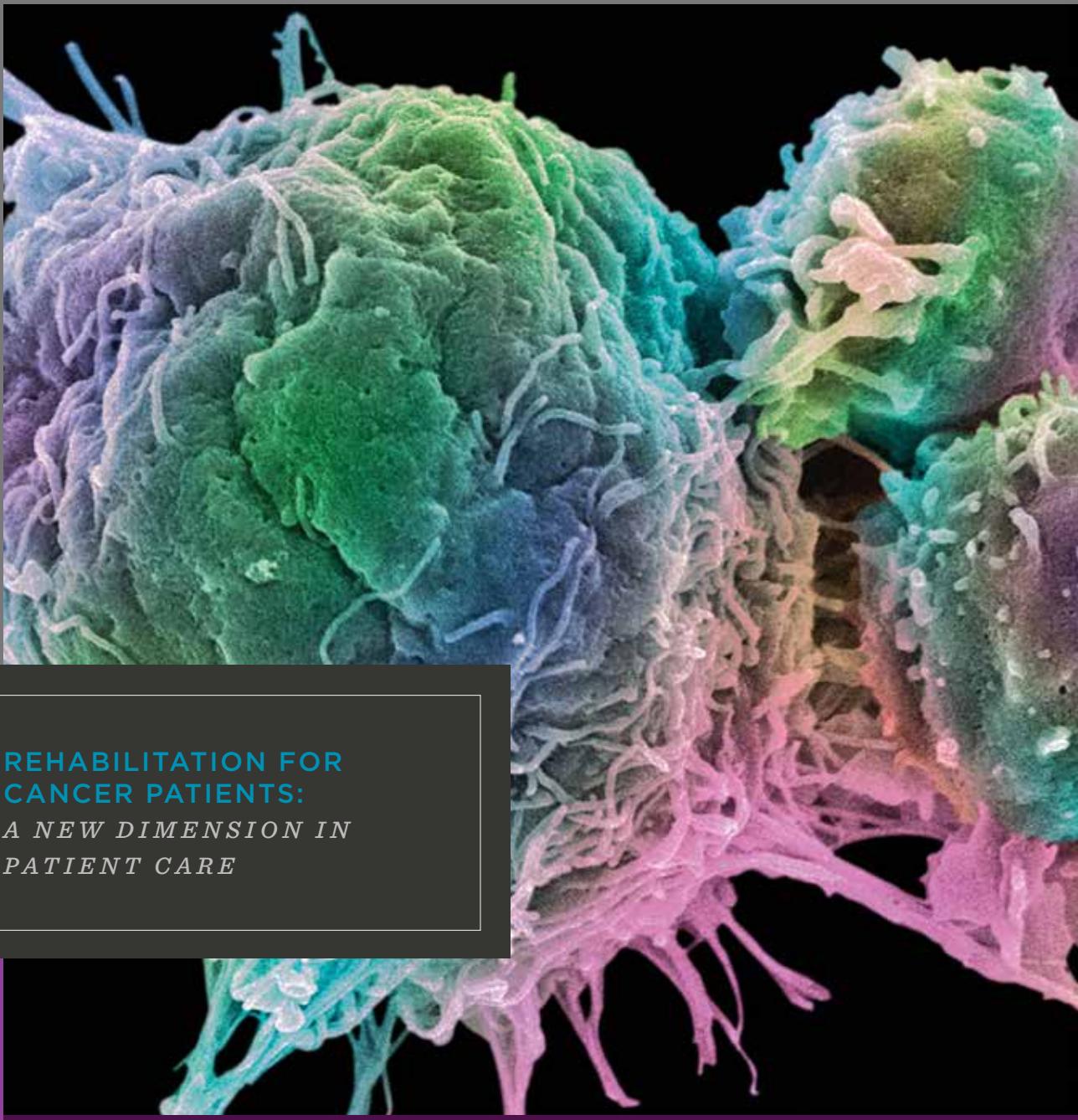
While it may be years or perhaps longer before the type of technology under investigation here leads to practical, everyday application for

individuals who have lost their ability to walk or move because of a traumatic spinal cord injury or other disorder or disease, the team's work has made great strides toward this goal in a relatively brief period of time. For Dr. Boninger, "In the end, what we're continuing to do is work toward restoring function. These incremental steps along that path are what we are building upon. In the absence of sensation, dexterous or complex tasks are next to impossible with vision alone. With incredibly talented researchers like Robert and Jennifer, Elizabeth Tyler-Kabara, Andy Schwartz, and our pioneering study participants, that path we are treading together is getting shorter."



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REHABILITATION FOR CANCER PATIENTS: *A NEW DIMENSION IN PATIENT CARE*

Individuals who have cancer have not consistently been a part of the patient population typically seen by physical medicine and rehabilitation physicians, in or outside the hospital. However, as cancer treatments have progressed over many years, with significant improvements in prognosis and survivorship, the ability of physical medicine and rehabilitation specialists to intervene and help restore lost function and preserve quality of life in these individuals is also on the rise.

Cancer takes significant physical tolls on a large percentage of those it afflicts. Be it from the cancer itself, or any of the accompanying therapies to treat it — radiation, chemotherapy, or surgical interventions — many patients suffer deficits in their functional ability and independence during and after treatment.

At the UPMC Rehabilitation Institute, Maryanne J. Henderson, DO, section chief for rehabilitation services at UPMC Shadyside, is leading several new initiatives to expand services and programs for individuals with cancer. Dr. Henderson sees a varied patient population, collaborating with oncologists both at UPMC Shadyside and the UPMC CancerCenter who refer inpatients from clinics, as well as working closely with therapists on the outpatient side of the care spectrum with UPMC Centers for Rehab Services (CRS).

"There are a number of therapists at CRS focused on cancer rehabilitation, and they are dealing with such things as lymphedema, myofascial release, certain neurological issues, and pelvic floor rehabilitation, and I work closely with them in the outpatient arena," says Dr. Henderson.

MULTIDISCIPLINARY COLLABORATIONS

Dr. Henderson currently has a weekly clinic for cancer patients at the UPMC Hillman Cancer Center. She treats breast cancer survivors with restricted range of motion in their shoulders due to surgery, scar tissue, and other complications. And there are a number of cases involving individuals with primary or metastatic brain lesions, often exhibiting symptomatology similar to those seen in cases of stroke — weakness on one side of the body and issues with balance.

Dr. Henderson has recently begun collaborating with a number of oncology specialists within the domains of head and neck cancer, surgical oncology, and survivorship to treat a range of patients. Dr. Henderson is also involved with the FRAILTY project, as well as the management of postsurgical scar and musculoskeletal disorders with oncology patients.



Dr. Henderson explains that in many cases patients receiving radiation therapy for their tumors will often end up with very stiff muscles and fibrosis leading to significant discomfort and painful loss of range of motion. Along with actively treating patients for their therapy needs, Dr. Henderson is quick to point out that she is in regular consult with the oncologists about her plans.

"I try very hard not to start any new medications without speaking to the oncologists to avoid any conflicts. Many of these patients are in studies or clinical trials, and I don't want to cause issues in that respect. To me, it's best to communicate with the oncologists and say, 'I'd like to start medication X, is that okay with you? Any objections?' It's an opportunity for us to connect and collaborate which, in the end, is best for the patient."

ADDRESSING MEDICALLY COMPLEX CASES

On the horizon for Dr. Henderson are initiatives to look at how best to treat medically complex cases — mostly neurological patients with significant brain or spinal cord involvement related to their cancer.

"We are looking at what is the best model of care. Should it even be in a rehabilitation unit when they are so medically fragile that they can't participate much in therapy? Or do we turn the tables on the idea, keep them in the hospital but increase their rehabilitation

exposure — taking more of a medical model than a rehabilitation model? This is something we are actively investigating."

AHEAD OF THE CURVE

Dr. Henderson explains that the whole idea of rehabilitation for cancer patients is really an emerging field, and UPMC has been ahead of the curve for several years in not only identifying the need but putting resources behind it. Dr. Henderson chairs the cancer rehab steering committee to help shape policy.

"It's exciting, because just five years ago rehabilitation for cancer patients was on few clinician's radar. Very few people were talking about it, and perhaps fewer, practicing. Today there are no accredited cancer rehabilitation fellowships, but I think that will change. We are seeing a recognition that there are benefits individuals can reap in inpatient rehabilitation after an acute care stay for cancer treatment, and on the outpatient spectrum as they continue to seek treatments and recover."





“We are seeing a recognition that there are benefits individuals can reap in inpatient rehabilitation after an acute care stay for cancer treatment, and in the outpatient spectrum as they continue to seek treatments and recover.”

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TRANSITIONS IN CARE: *SHORT DURATION REHABILITATION*

As the world of rehabilitation medicine changes alongside the continually evolving universe of the broader health care environment, the UPMC Rehabilitation Institute has taken strides to fill a gap in rehabilitation services for a subset of patients who require short duration rehabilitative care. These patients can no longer stay in an acute care hospital environment, but they also are not yet ready to return home.

Enter the Transitional Rehabilitation Units (TRUs) into the larger world of the UPMC Rehabilitation Institute's continuum of care. Also enter Natasa Miljkovic, MD, PhD, assistant professor and the new medical director of rehab services in the TRUs as of July 2016. Dr. Miljkovic sees the transitional rehabilitation care provided through the TRUs as the ideal bridge for patients who need some form of rehabilitation, but who do not necessarily fit into the existing models of care provided by acute inpatient rehabilitation, or traditional skilled nursing and rehabilitation facilities.

The TRUs are purpose-built for individuals who have had an injury or who were hospitalized for reasons such as a surgery, trauma, or even a mild stroke. "These patients do need some rehabilitation, and though they do not need as intense a regimen as inpatient rehabilitation, they need more than the typical one-hour-a-day they receive in skilled nursing facilities," says Dr. Milkovic.

The length of stay for patients in the TRU averages approximately two weeks, and each patient has a detailed, individualized plan of care developed to meet their specific needs, as well as their overall goals for recovery. The goal is to have patient care at each of the TRU facilities coordinated by a physical medicine and rehabilitation physician from the department, with Dr. Miljkovic providing coordination and oversight over the entire network of TRUs.

Dr. Miljkovic and the other rehab physicians at the TRUs work closely with each patient, their primary care provider, and the staff at the skilled nursing facility to ensure optimal outcomes. "We are involved in their care as physical medicine and rehabilitation doctors. We can shape individualized rehab programs according to their functional goals and needs, and if there are barriers to rehab noted by the physical or occupational therapists, they



always approach us and we work together to overcome the problem and maximize the effects of rehabilitation for the patient."

AN INTERCONNECTED NETWORK

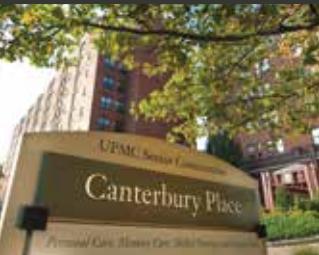
Currently, the UPMC Rehabilitation Institute operates four TRU locations around the greater Pittsburgh area. The dedicated units are located within existing skilled nursing facilities operated by UPMC Senior Communities, a large collection of independent and assisted living residences for seniors, and a network of skilled nursing facilities. There are currently a total of 140 beds for TRU patients, and in November 2016, a 17-bed cardiac patient-specific unit began accepting patients at UPMC Canterbury Place. Dr. Miljkovic will oversee rehab services at this unit as well, working in conjunction with partners from the UPMC Heart and Vascular Institute.

The TRU units in each building have all undergone recent redesigns, remodeling, and in some cases, expansion to improve the areas for patients and staff, providing enhancements for their comfort as well as their rehabilitation.

TRANSITIONAL REHABILITATION UNITS BY FACILITY(AS OF 11/16)

Canterbury Place

**36
BEDS**



Cranberry Place

**30
BEDS**



Heritage Place

**24
BEDS**



Seneca Place

**50
BEDS**



CONTINUITY OF CARE

A goal of Dr. Miljkovic for the TRUs and its patient population is to ensure that every patient referred to one of the units and seen in the acute care hospital by one of the PM&R physicians is followed by a PM&R physician at the TRU as well. This will provide a level of continuity of care that has not existed in the past. "This isn't easy and we're not there just yet. We are building a network of people, including case managers and rehab liaisons, to help us identify where the patient was discharged from acute care and make sure that we continue to follow the ones who would benefit greatly from being cared for by a PM&R physician," says Dr. Miljkovic.

PARTNERS IN CARE FOR BETTER OUTCOMES

At the heart of Dr. Miljkovic's patient care philosophy are a deep appreciation of cross-discipline collaboration and an attention toward the geriatric population. In the TRUs, Dr. Miljkovic and her team collaborate with the primary care physicians, and, depending on the patient, with their geriatrician. This collaborative model is, Dr. Miljkovic believes, the model that the broader world of patient care is moving toward, and one that she intends to follow.

Within the skilled nursing facilities, the reach and ability of the rehabilitation physicians to influence and assist with patient care

goes beyond the TRUs. "Our colleagues in internal medicine, geriatricians and nurse practitioners, are finding more and more patients who could benefit from seeing us, not only in the TRUs but also in long-term care," says Dr. Miljkovic. She and the other unit directors are working to apply their knowledge and expertise in physical medicine to the entire skilled nursing facility. "In the end, it's our collaborations with the patient's entire care team that will make the difference when it comes to quality of care and the many values one can place on that."

ASSISTING PATIENTS WITH COGNITIVE CHALLENGES

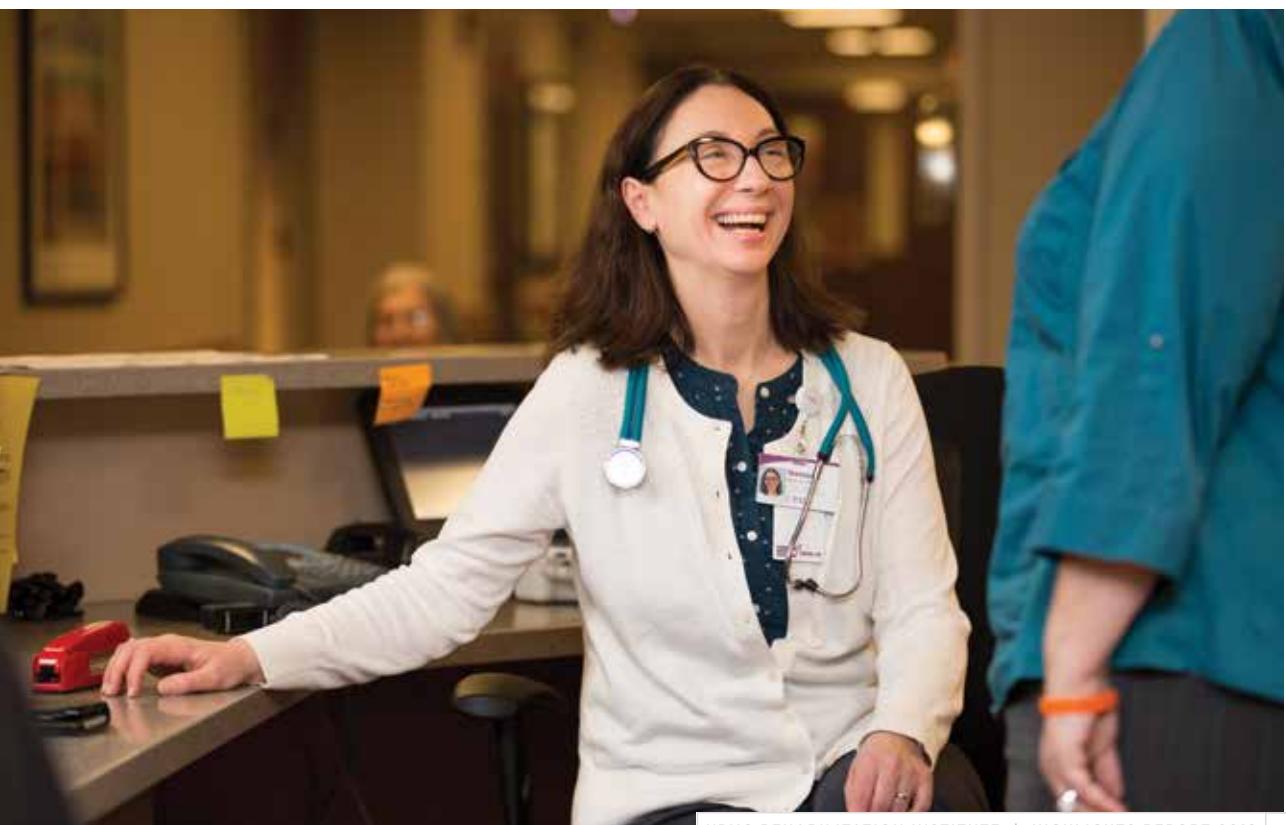
Dr. Miljkovic sees a natural place for physical medicine and rehabilitation in the world of memory care. Within the skilled nursing of UPMC Senior Communities, several of the facilities offer dedicated memory care units for patients with cognitive and memory impairment from such conditions as Alzheimer's disease. Another of Dr. Milkovic's goals for the future is to offer her services to individuals with dementia. For those with mild or moderate dementia, "the literature shows that you can have positive results with physical therapy, occupational therapy, and cognitive rehabilitation." In a way, it makes perfect sense. A diagnosis of dementia, whatever the cause, doesn't cancel out a person's other physical conditions or functioning. "My goal is to be available to each and every resident in

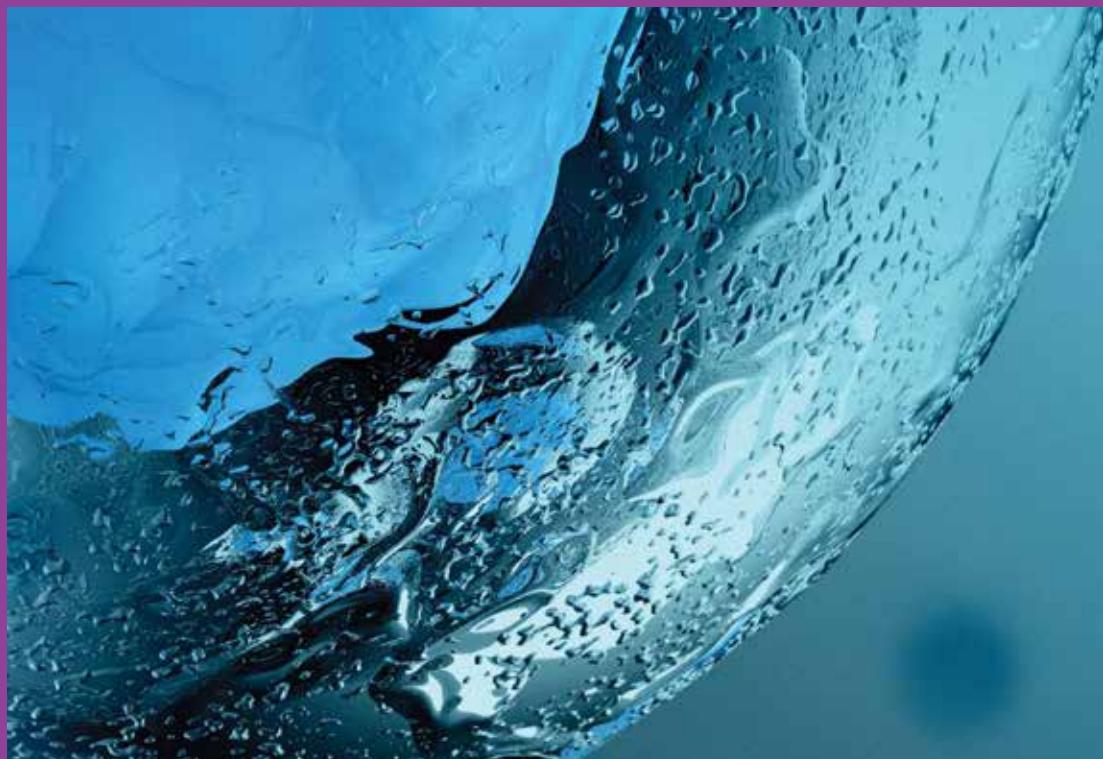
those facilities regardless of diagnosis. Everybody deserves a chance to live life fully and maximize their functional potential, including people with dementia," says Dr. Miljkovic.

FUTURE PLANS

Improving upon, and expanding patient services is, and will continue to be, a priority for Dr. Miljkovic. For Dr. Miljkovic, the older adult population continues to be of great interest — in terms of research, her own clinical care, and her collaboration with the world of geriatrics and gerontology. In this patient population, she is primarily interested in how to keep the geriatric patient maximally functional for as long as possible. Dr. Milkovich envisions a geriatric clinic where there is a focus on fall prevention and performing functional evaluations of older adults to assess where on the functional spectrum an individual rests, their capabilities, and, whether or not changes in living situations may be warranted, for example, when to move an

individual from independent living to assisted living, and similar quality of life decisions. While not part of her current clinical duties, Dr. Miljkovic does hope to develop such a clinic in the future. Given the aging population, these kinds of services will no doubt be in short supply, and in high demand. Another expansion program that Dr. Miljkovic would like to design and implement are inpatient rehabilitation services for individuals with mild to moderate dementia. Dr. Miljkovic explains the concept with an example. "Take for instance an individual with mild or moderate dementia who is still living at home and, perhaps, not totally self-sufficient, but still able to function with supervision and care. This individual suffers a fall, fractures a hip, and is hospitalized for a surgery. Their rehabilitation needs coupled with their dementia needs create a challenging set of circumstances. Right now, this specialized kind of care does not exist." One day, however, this type of resource may just become a routine type of care, and Dr. Miljkovic will be leading the way forward.





REGENERATIVE REHABILITATION: *AN INTERSECTION OF DISCIPLINES*

The burgeoning field of regenerative medicine and related technologies takes many forms and follows a multitude of investigational avenues. And this research and related technologies are quickly making an impact on clinical practice. Regenerative rehabilitation is one of these fields. The intersection of physical medicine and rehabilitation (PM&R) and regenerative medicine combines the strengths of PM&R and its ability to tap into the body's endogenous healing capacities with regenerative medicine technologies, such as tissue engineering, cellular therapies, and biomaterials. The ultimate goal of regenerative rehabilitation is to translate this research into clinical practice to maximize functional outcomes for patients.

A leader in this relatively new yet expanding field is Fabrisia Ambrosio, PhD, MPT, associate professor of physical medicine and rehabilitation and recently appointed director of rehabilitation for UPMC International. Dr. Ambrosio holds secondary appointments in the departments of Physical Therapy, Orthopaedic Surgery, Bioengineering, and Microbiology & Molecular Genetics. Dr. Ambrosio's research is focused on skeletal muscle healing and functional recovery, and she pursues this research through multiple channels, looking for ways to restore function through the repair or regeneration of damaged or lost tissues, augmented by rehabilitation protocols that use physical and mechanical means to promote recovery.

"The primary focus of our laboratory is skeletal muscle and, specifically, investigating the biology underlying declines in regenerative potential due to aging and disease. In addition, we're very interested in how mechanical stimulation protocols may be used to prevent or counteract these declines," explains Dr. Ambrosio.

In terms of cellular therapies for the restoration of function after injury or disease, Dr. Ambrosio seeks to understand the possibilities of rehabilitating transplanted cells as a means to enhance the survival and engraftment of the donor cells after transplantation, a large challenge with cellular therapeutics in general.

"In this respect, our goal is to use rehabilitation protocols as a way to communicate with the cells even after transplantation and to facilitate incorporation into the host tissue in a more functionally relevant manner," says Dr. Ambrosio.



And, indeed, what she and her colleagues have found through the course of several recent and ongoing studies is that in the case of myopathies, as well as very severe muscle injuries, when a rehabilitation protocol is added to stem cell transplant paradigms, it results in better transplantation efficiency. Cellular behavior occurred more in the manner that was intended, migrating throughout the tissue, forming new muscle, and showing the results to be functionally relevant.

Studies of this nature have shown Dr. Ambrosio and her colleagues that the synergies created between cellular therapies and rehabilitation protocols can pull the two fields together. "The whole is greater than the sum of the parts. Rather than continue to pursue various approaches in a parallel stream, we're interested in merging the two fields as a means of accelerating research and translational progress."

CURRENT RESEARCH HIGHLIGHTS

While Dr. Ambrosio and her lab's research portfolio is large and continues to expand, two recent studies shine light on how the field is advancing and to its inherently collaborative, multidisciplinary approach to complex translational research.

Volumetric Muscle Injuries

In a Department of Defense (DOD) funded clinical trial, Dr. Ambrosio collaborated with University of Pittsburgh principal investigators, Steven Badylak, MD, PhD, DVM, and J. Peter Rubin, MD, FACS, on a tissue engineering approach for the treatment of volumetric muscle injuries. Volumetric muscle injury, for this particular study, was defined as involving at least 25 percent loss of muscle mass, as well as 25 percent loss of muscle function. These injuries are common on the battlefield through blast trauma or other means. Individuals recruited into the study, for the most part, had exhausted all other treatment options. They had undergone multiple surgeries, multiple different approaches to try and restore their function, and yet they still had considerable functional deficits. "The idea behind the study was to use a tissue engineering approach to try and promote a constructive remodeling of the injury site through the implantation of an acellular extracellular matrix scaffold. We complemented that with a rehabilitation protocol which was initiated one day after implantation of the device," says Dr. Ambrosio. Results from this study¹ were recently published in the journal *npj Regenerative Medicine*, and showed, among other findings that biological scaffolds implanted to treat volumetric muscle injuries increased skeletal muscle force production and functional outcomes post-surgery.

Stroke Research

More recently, Dr. Ambrosio has begun collaborating with Michael Modo, PhD, associate professor in the Department of Radiology. The two investigators were looking at very similar paradigms in the case of cellular therapeutics for the treatment of stroke. Specifically, Drs.

Modo and Ambrosio are evaluating whether, and how, varying training regimens may promote the therapeutic benefit of stem cells transplanted into rats after an acute infarction event.

ANNUAL INTERNATIONAL SYMPOSIUM ON REGENERATIVE REHABILITATION

In 2011, Dr. Ambrosio helped to organize, and continues to lead, the Annual International Symposium on Regenerative Rehabilitation. Heading into its sixth year, this annual event brings together researchers and clinicians from around the globe to learn about and share their research and emerging trends from within the field.

The two-day symposium, which is accredited for AMA PRA Category 1 Credit(s)TM, features an array of workshops, presentations, poster sessions, and thematic lecture sessions by many of the leading figures in regenerative medicine and physical medicine and rehabilitation.

The 2017 symposium will occur November 1-3 in Pittsburgh, Pennsylvania, and is being co-hosted by the University of Pittsburgh and Kyoto University. "This year's symposium will be larger than in year's past, and with a greater international presence," says Dr. Ambrosio.

For a recap of the 2016 symposium, and for details about the 2017 symposium or other upcoming events, please visit www.ar3t.pitt.edu/symposium.

ASSEMBLING A CONSORTIUM TO ADVANCE THE DISCIPLINE

From the development of the symposium has grown an International Consortium on Regenerative Rehabilitation (ICRR) created by Dr. Ambrosio and her colleagues at the University of Pittsburgh and the Palo Alto VA Rehabilitation R&D REAP Center. In only a few short years, ICRR has grown to include 11 institutions in North America, Asia, and Europe. "It's been exciting to see the momentum that the field is receiving and the widespread support from all over the world," says Dr. Ambrosio.

A close-up photograph of a woman with long brown hair, wearing a white lab coat over a blue top. She is looking directly at the camera with a slight smile. In her hands, she holds a petri dish containing several small, colorful samples, possibly tissue cultures or genetic constructs, arranged in a grid. The background is slightly blurred, showing another person in a lab setting.

“The primary focus of our laboratory is skeletal muscle and specifically, investigating the biology underlying declines in regenerative potential with aging and disease.”



Dr. Ambrosio (center), along with lab colleagues (l-r) Veronica Santos, Amrita Sahu, Sunita Shinde, and Hikaru Mamiya

The ICRR is pushing the field forward by developing a strategic plan for the International Symposium and other initiatives it is undertaking. Ultimately, the Consortium seeks to expand the research and clinical applications of regenerative rehabilitation through educational initiatives, research, pilot grant funding, and advocacy initiatives.

AR³T AND EDUCATIONAL OPPORTUNITIES FOR RESEARCH AND LEARNING

A new, NIH-funded multicenter collaborative — the Alliance for Regenerative Rehabilitation Research and Training (AR³T) — is working to expand scientific knowledge, expertise, and methodologies across the domains of rehabilitation science and regenerative medicine. Dr. Ambrosio is a co-investigator of the Alliance, along with primary investigators Michael Boninger, MD (University of Pittsburgh), and Thomas A. Rando, MD, PhD (Stanford University) and other co-investigators Linda Noble-Haeusslein, PhD (UCSF),

Carmen Terzic, MD, PhD (Mayo Clinic), and Gwendolyn Sowa, MD, PhD (University of Pittsburgh). For clinicians and researchers desiring to learn even more about Regenerative Rehabilitation, Dr. Ambrosio and her colleagues have developed a number of initiatives to facilitate ongoing education and research opportunities.

An Advanced Training Course was created in 2016 for rehabilitation specialists seeking to learn more about, or desiring to move into, the field of regenerative rehabilitation. This week-long, intensive course highlights the cutting-edge science being conducted in the field, but also gives participants some initial laboratory experience. The last course (in June, 2016) saw participants culturing induced pluripotent stem cells. This National Institutes of Health-sponsored course, co-directed by Dr. Ambrosio and Gerald P. Schatten, PhD, professor and vice chair of Obstetrics, Gynecology, and Reproductive Sciences and director of the Division of Developmental and Regenerative Medicine, is designed to attract new talent to the field with intensive, hands-on learning.

For established researchers, sabbatical opportunities are available in a partnership between the University of Pittsburgh, Stanford University, the Mayo Clinic, and University of California San Francisco. The four institutions provide fully-funded sabbatical opportunities for researchers to visit and work at the facilities of one of the partners. Dr. Ambrosio indicates that this partnership is designed to help individuals grow their regenerative rehabilitation programs at their own institutions, and to advance the field as a whole.

Additionally, there is a free, quarterly webinar series for viewing and learning, and the AR³T supports new research through pilot grant funding. All of these initiatives add up to show how Dr. Ambrosio and the UPMC Rehabilitation Institute are leading the growth and advancement of regenerative rehabilitation medicine around the world.

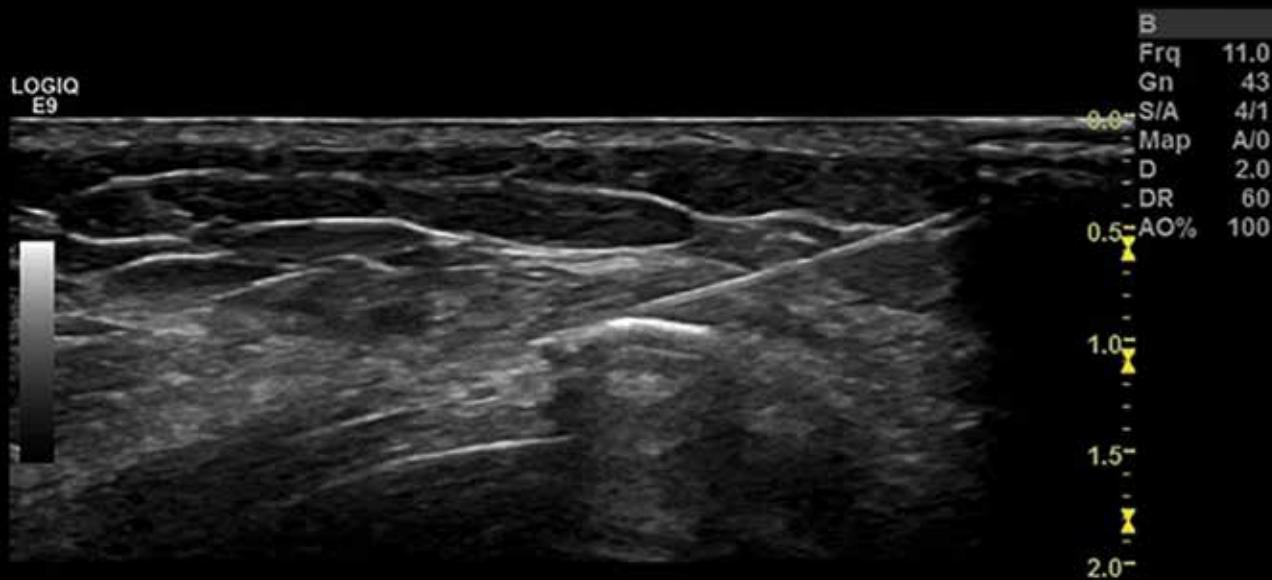


Culture plates used to expand and characterize muscle stem cells.

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RIGHT IT BAND INJ



**NEW TRENDS IN
REHABILITATION MEDICINE:
*ULTRASOUND AS A CLINICAL
AND RESEARCH TOOL***

For Kentaro Onishi, DO, assistant professor and incoming director of the ACGME-accredited Sports Medicine Fellowship, the role of ultrasound imaging and its use in ultrasound-guided injections and nonsurgical interventions, and as a tool for research in rehabilitation medicine and orthopaedic surgery, continues to expand.

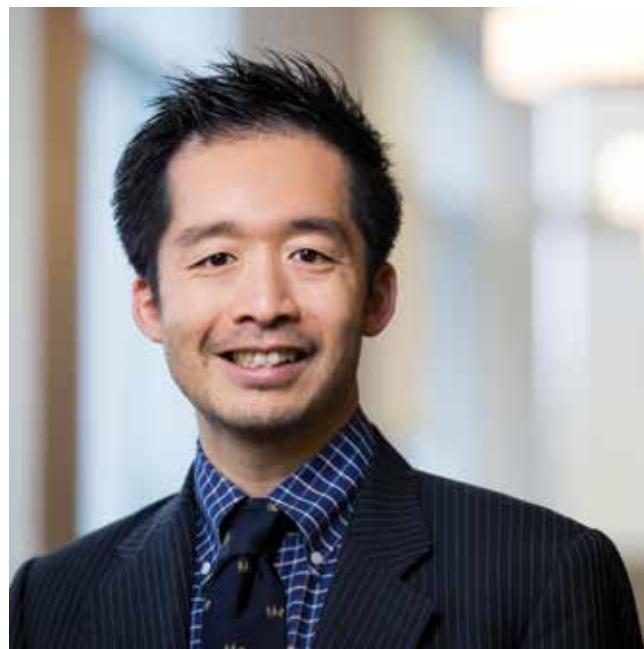
Since arriving at the UPMC Rehabilitation Institute in September 2015, Dr. Onishi has worked to establish a growing clinical practice focusing on integration of diagnostic ultrasound and nonsurgical sports medicine procedures for patients using ultrasound-guided techniques in the outpatient setting, as well as regenerative and orthobiologic treatments including platelet-rich plasma and stem cell injections. An avid runner himself, Dr. Onishi understands the special needs of athletes. For a certain subset of applicable patients with tendinopathies or plantar fasciopathy, Dr. Onishi performs FDA-approved Tenex™ procedures in his clinic, as well as ultrasound-guided “tendon scraping” procedures, which require minimal down-time before return to sports.

Dr. Onishi also is involved in a growing body of research efforts, lending his talents and expertise in musculoskeletal (MSK) ultrasound to colleagues in the Department of Physical Medicine and Rehabilitation, as well as those from the Department of Orthopedic Surgery and UPMC Sports Medicine as they investigate a range of conditions and therapeutic approaches. “Musculoskeletal ultrasound is a great research, as well as clinical tool,” says Dr. Onishi. The approaches he is using in the clinic and the lab represent a new horizon in research circles and in the world of sports medicine.

ULTRASOUND IMAGING AS A DIAGNOSTIC TOOL

Dr. Onishi’s clinical practice is focused on diagnostic ultrasound, whereby ultrasound is used to visualize structures and help to determine causative reasons for a patient’s pain or other symptoms. Alongside a thorough patient examination, history, and other diagnostic elements, diagnostic ultrasound adds another layer of clarity to cases — be it those requiring surgical intervention, or helping to identify candidates for less invasive, nonsurgical interventions or procedures.

“Ultrasound imaging is becoming more accepted with my sports medicine colleagues where it can sometimes assist in the decision-making process. There are cases where an MRI comes back negative, and ultrasound with its superior spatial resolution can sometimes pinpoint issues MRI cannot,” says Dr. Onishi.



Dr. Onishi routinely receives requests from his colleagues to image a patient for them. These findings are incorporated into their surgical planning, to aid in devising appropriate treatment options with this diagnostic data that can help to fill in a particular patient’s clinical picture and assessment. “It’s a collaborative process, and the benefits for the patient needing the surgery can be significant,” indicates Dr. Onishi.

ULTRASOUND-GUIDED INTERVENTIONS AND INJECTION THERAPIES

While ultrasound is a powerful diagnostic tool, its application to clinical procedures is well documented. The ability to perform ultrasound-guided interventions is a very

discrete skill set and requires advanced training in both ultrasound interpretation and techniques, and in knowledge of the anatomy.

In the clinic, Dr. Onishi is able to use ultrasound to guide a number of procedures for patients with tendon injuries and other conditions. These include percutaneous sonographically-guided tendon scraping procedures for chronic conditions such as Achilles tendinosis, and percutaneous ultrasonic tenotomy and fasciotomy and debridement (known as TENEX procedure). He also is able to perform ultrasound-guided injections of such things as platelet-rich plasma for the treatment of tendon and joint conditions.

Performing the injections and other procedures under sonographic guidance significantly increases accuracy of procedures and safety for the patients. As an example of how ultrasound guidance can improve injection accuracy, Dr. Onishi explains that, "Under no guidance, injecting shoulder joints can lead to a higher chance of missed injections.³ With that high of a percentage, trying to ascertain clinical significance of the treatment is problematic." Dr. Onishi and colleagues are currently designing a clinical study using ultrasound guidance to ascertain the efficacy of biological agents derived from adipose-tissue for shoulder arthritis.

ULTRASOUND IMAGING AND ITS ROLE IN RESEARCH: INTERESTS AND COLLABORATIONS

Ultrasound and ultrasound-guided procedures are of benefit not only in the world of clinical practice of physical medicine and rehabilitation, but in research and collaboration with such areas as sports medicine and orthopaedic surgery. Beyond his clinical practice, Dr. Onishi has an active research portfolio and is lending

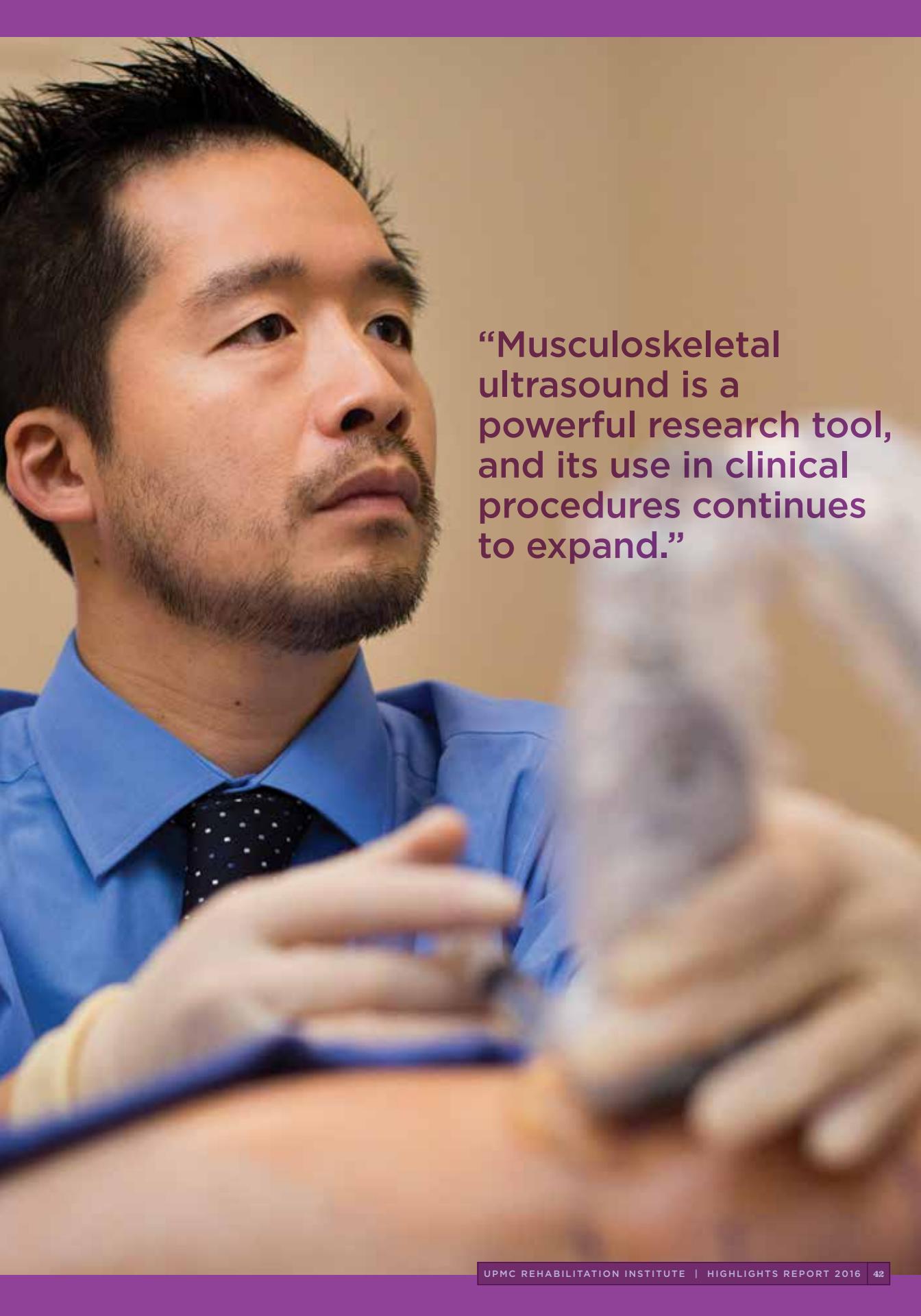
his talents in ultrasound-guided approaches to colleagues in the Department of Orthopaedic Surgery.

Stem Cell Viability After Injection

Stem cells and stem cell therapies are of clinical interest to Dr. Onishi as treatment approaches to various conditions and injuries, and an avenue of investigation he continues to pursue in the lab. In the recent past, Dr. Onishi has investigated what, if any, detrimental biological effects occur to stem cells during the physical process of injection via different gauge needles. Dr. Onishi was interested to learn what might be happening to the cells in the narrow confines of the needle related to the mechanical stresses of the injection process. Do the cells die off in large numbers because of the physical stress and mechanics of injection, or do they change in other ways, rendering their potency or ability to heal less than optimal? "Until we published our study, there was little information out there on the cellular effects, or possible cell death rates, as part of the physical act of injecting stem cells through a needle into host tissues," says Dr. Onishi.

Dr. Onishi's study¹ looked at adipose/fat-derived mesenchymal stromal stem cells injected through both 18-gauge and 30-gauge needles with similar concentrations of cells and with similar rates of flow through the needles. Results of the experiments showed several important findings. While cellular metabolic activity was changed, potency, cellular proliferation capacity, and overall cell viability was relatively unchanged after passage through both gauge needles.

"Cellular identity was virtually identical before and after the injections. This is important because we now know that stem cells can be injected with a 30-gauge needle without compromising the cell, and this can be useful information for those who practice stem cell injection therapy."

A close-up photograph of a man with dark hair and a beard, wearing a blue dress shirt and a dark tie with white polka dots. He is focused on performing a medical procedure on a patient's shoulder. His hands are positioned on the patient's back and shoulder area, holding a handheld ultrasound probe. The patient's arm is visible, extending from the bottom right towards the center. The background is blurred, suggesting a clinical setting.

“Musculoskeletal ultrasound is a powerful research tool, and its use in clinical procedures continues to expand.”

ORTHOPAEDIC SURGERY COLLABORATIONS

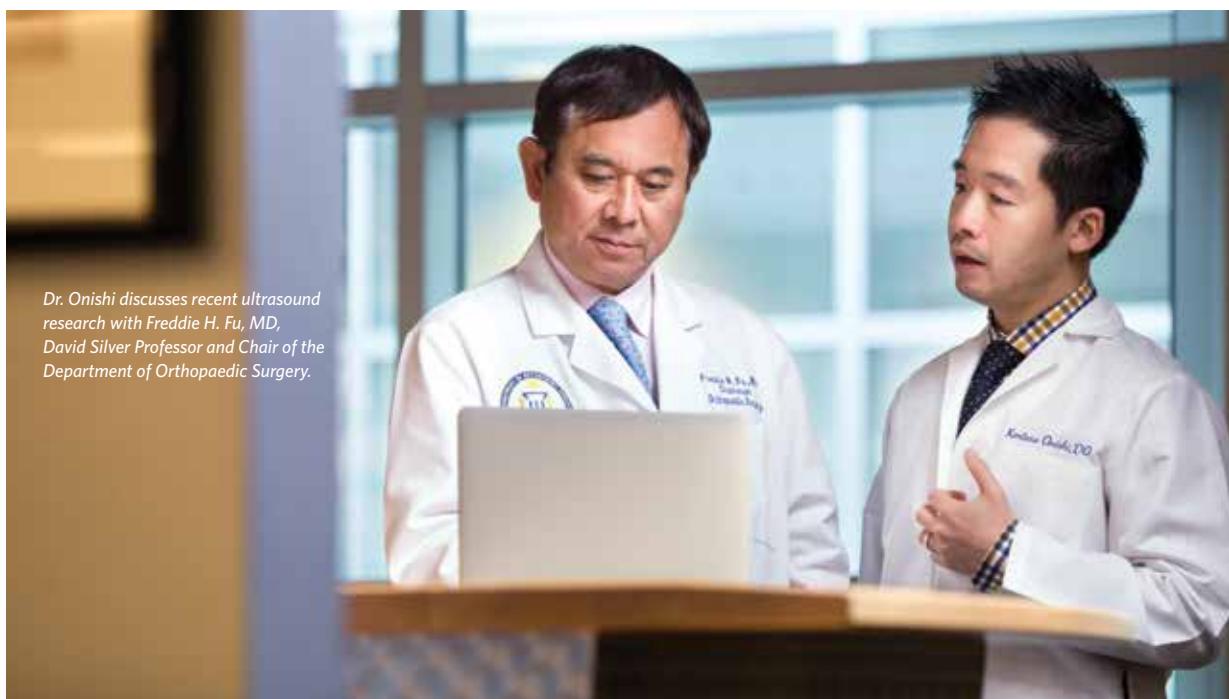
Dr. Onishi has collaborated recently with several individuals in the Department of Orthopaedic Surgery, including department chairman, Freddie H. Fu, MD, on studies of the anterolateral complex of the knee designed to bring forth a better understanding, and visualization, of the structures that make up this area.

Ultrasound-Guided Catheter Insertion and MuscleSound

Dr. Onishi and colleagues have two current research studies under way using ultrasound. The first involves the development of a technique to measure the inflammatory status of the glenohumeral joint using microdialysis.

Ultrasound is used to guide the insertion of the catheter into the posterior aspect of the glenohumeral joint, allowing Dr. Onishi and his study collaborators to determine the optimal placement of the catheter, and to guide it into place without damaging shoulder stabilizing structures or joint cartilage.

The second investigation in collaboration with Takashi Nagai, PhD, assistant professor in the Department of Sports Medicine and Nutrition in the School of Health and Rehabilitation Sciences, is a two-part study designed to establish the inter/intra reliability of the ultrasound-based MuscleSound™ system designed to capture muscle glycogen measurements, as well as to evaluate the effects of fatigue induced by intermittent running on muscle glycogen.



Dr. Onishi discusses recent ultrasound research with Freddie H. Fu, MD, David Silver Professor and Chair of the Department of Orthopaedic Surgery.

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PATIENT OUTCOMES

PATIENT OUTCOMES

JULY 1, 2015 TO JUNE 30, 2016

All Patients

| <i>Key Outcome Indicators</i> | <i>UPMC Rehabilitation Institute</i> | <i>Nation (Acuity Adjusted)</i> | |
|-------------------------------|--------------------------------------|---------------------------------|----------------------|
| Number of Patients | 4,480 | | |
| FIM change per day | 2.58 | 2.27 | Higher is better |
| Average admission FIM™ | 54.5 | 58 | Lower = more complex |
| Discharge to community | 72% | 72% | Higher is better |
| ALOS (days) | 14.3 | 14.5 | |

Source: UDSMR® Time frame: July 1, 2015 to June 30, 2016

Stroke Patients Only

| | | | |
|------------------------|-------|------|----------------------|
| Number of Patients | 1,253 | | |
| FIM change per day | 2.29 | 1.93 | Higher is better |
| Average admission FIM™ | 48.5 | 52.4 | Lower = more complex |
| Average FIM change | 30.1 | 26.8 | Higher is better |
| Discharge to community | 65% | 67% | Higher is better |
| ALOS (days) | 15.8 | 16.6 | |

Source: UDSMR® Time frame: July 1, 2015 to June 30, 2016

Brain Injury Patients Only (traumatic and nontraumatic)

| <i>Key Outcome Indicators</i> | <i>UPMC Rehabilitation Institute at UPMC Mercy</i> | <i>Nation (Acuity Adjusted)</i> | |
|-------------------------------|--|---------------------------------|-----------------------|
| Number of patients | 317 | | |
| Case mix index | 1.67 | 1.26 | Higher = more complex |
| FIM change per day | 2.61 | 2.13 | Higher is better |
| Average admission FIM | 37.6 | 46.7 | Lower = more complex |
| Average FIM change | 35.8 | 29.7 | Higher is better |
| Discharge to community | 66% | 66% | Higher is better |
| ALOS (days) | 18 | 16.3 | |
| Admission Cognitive FIM | 10 | 16.3 | Lower = more complex |

Source: UDSMR® Time frame: July 1, 2015 to June 30, 2016

Spinal Cord Injury Patients Only (traumatic and nontraumatic)

| | | | |
|-------------------------|------|------|-----------------------|
| Number of patients | 261 | | |
| Case mix index | 2.06 | 1.46 | Higher = more complex |
| FIM change per day | 2.08 | 1.59 | Higher is better |
| Average admission FIM | 47 | 50.9 | Lower = more complex |
| Average FIM change | 34.9 | 26.6 | Higher is better |
| Discharge to community | 65% | 62% | Higher is better |
| ALOS (days) | 21.3 | 21.7 | |
| Admission Cognitive FIM | 23.2 | 25.8 | |

Source: UDSMR® Time frame: July 1, 2015 to June 30, 2016

KEY

The FIM™ instrument is a measure of disability. The scale measures the ability to carry out an activity independently, against the need for assistance from another person or device. Lower FIM scores mean greater dependence. The need for assistance, or burden of care, translates to the time and energy that another person must expend to serve the needs of the disabled individual so that they can achieve and maintain a certain quality of life.

The FIM instrument measures the following domains:

- Self-care
- Bladder/bowel management
- Transfers
- Mobility/locomotion
- Cognition

Case mix index — the acuity level of patients

FIM change per day — average FIM change per day

Average admission FIM — total score for all FIM categories at time of admission

Average FIM change — difference between admission and discharge FIM scores

Discharge to community — percentage of patients discharged to their homes

ALOS — average length of stay for patients in this impairment category

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