Institution: Manchester Metropolitan University

Unit of Assessment: A3 Allied Health Professions, Dentistry, Nursing and Pharmacy

Title of case study: Musculoskeletal Responses To Spaceflight: Exercise Countermeasures Developed From MMU Research

1. Summary of the impact

This case study relates to Manchester Metropolitan University (MMU) research on musculoskeletal responses to microgravity conditions in spaceflight and the resulting applications and impacts. MMU's research and influence within the UK Space Biomedicine Consortium underpinned a shift in UK Government policy towards full participation in European Space Agency (ESA) programmes. Impacts have also resulted from the development of gravity-independent devices and exercise systems that have been tested by ESA and NASA within various "live" missions on board the International Space Station. MMU's research has also had a big influence on the organisational practices of the German Aerospace Centre (DLR) particularly around space physiology.

2. Underpinning research

Microgravity adversely affects the muscles, bones and tendons of the human body and so the stresses associated with spaceflight can have a potentially serious effect on astronauts and their ability to carry out missions safely. Solutions are badly needed to overcome harmful musculoskeletal responses as the average "space time" of missions increases. Research findings from spaceflight have important clinical applications in the "real world" and MMU's research in particular is supporting the development of rehabilitation and vibration techniques to combat muscle deterioration.

The underpinning research in this case study was conducted by MMU researchers: Professor Joern Rittweger (MMU 2003-Present), Professor Neil Reeves (MMU 2003-Present), Professor Marco Narici (MMU 1999-2012) and Professor Costis Maganaris (MMU 2000-2012). The research team pioneered non-invasive techniques based on combining ultrasound imaging and dynamometry to study the behaviour of muscles and tendons in vivo. These techniques were applied to study the effects of various microgravity simulation paradigms, such as bed-rest and lower limb suspension, on the musculoskeletal system leading to a number of published papers in major international journals. Findings showed for the first time how human tendons would decrease their mechanical stiffness (via deterioration of the material properties of the tendon) and bone mineral content was reduced in response to a prolonged period of simulated microgravity (90 days of bed-rest) **[3, 4]**. Research showed for the first time that the internal architecture (structure) of the muscle was affected along with a reduction of the gross size of the muscle **[1, 2]**. Professor Rittweger pioneered the application of resistive vibration exercise as an effective countermeasure for preventing muscle and bone loss due to microgravity exposure **[5, 6]**. Based on previous experience in acute and chronic responses to vibration exercise, a training regimen was developed that was the first to achieve full efficacy to prevent structural bone deficits in the tibia, i.e., the site of greatest bone loss in simulated microgravity.

Between 2001 and 2002, the MMU research team took part in a series of microgravity simulation studies (around long-term bed rest) organised by the European Space Agency (ESA). ESA is an inter-governmental organisation dedicated to the exploration of space and therefore the collaboration around this research had impact embedded from the outset. The research involved testing the efficacy of a 'Yo-Yo Flywheel Ergometer' in preventing muscle atrophy, tendon deconditioning and bone loss. They elucidated the effects of simulated microgravity on the musculoskeletal system and the efficacy of the 'Yo-Yo Flywheel Ergometer' in preventing its deterioration. This work resulted in a number of publications **[3, 4,]** that directly influenced the decision of ESA and NASA to fly the 'Yo-Yo Flywheel Ergometer' to be evaluated as part of the Human Research Facility on the International Space Station (ISS) in 2009/10. Findings have also been used to combat the negative effects of muscle deterioration and bed-rest in clinical applications across Europe.

3. References to the research

[1] Narici MV, Maganaris CN & Reeves ND. (2002). Muscle and tendon adaptations to ageing and spaceflight. Journal of Gravitational Physiology 9, 137P-138P.

[2] Reeves ND, Maganaris CN, Ferretti G & Narici MV. (2002). Influence of simulated microgravity

on human skeletal muscle architecture and function. Journal of Gravitational Physiology 9, 153P-154P

[3] Reeves ND, Maganaris CN, Ferretti G & Narici MV. (2005). Influence of 90-day simulated microgravity on human tendon mechanical properties and the effect of resistive countermeasures. Journal of Applied Physiology 98, 2278-2286. **DOI:** 10.1152/japplphysiol.01266.2004 *(75 citations)*

[4] Rittweger J, Frost H, Schiessl H, Ohshima H, Alkner B, Tesch P & Felsenberg D (2005). Muscle atrophy and bone loss after 90 days' bed rest and the effects of flywheel resistive exercise and Pamidronate: Results from the LTBR study. Bone 36, 1019-1029.
DOI: 10.1016/j.bone.2004.11.014 *(93 citations)*

[5] Blottner D, Salanova M, Püttmann B, Schiffl G, Felsenberg D, Buehring B & Rittweger J. (2006). Human skeletal muscle structure and function preserved by vibration muscle exercise following 55-days of bed rest. European Journal of Applied Physiology 97, 261-271 http://www.ncbi.nlm.nih.gov/pubmed/16568340 *(94 citations)*

[6] Mulder ER, Stegeman DF, Gerrits KHL, Paalman MI, Rittweger J, Felsenberg D & de Haan A. (2006). Strength, size and activation of knee extensors followed during 8 weeks of horizontal bed rest and the influence of a countermeasure. European Journal of Applied Physiology 97, 706-715.
DOI: 10.1007/s00421-006-0241-6 *(48 citations)*

Indicators of Research Quality

The following peer-reviewed funding has supported the above work:
€11.2 million - European Union FP7 grant 'Myoage' (contract No: 223576). Awarded to Prof. Marco Narici (PI). 2009-2013
€546,000 - European Space Agency grant (ESA MAP project grant 14737/NL/SH). Co-ordination by Prof. Per Tesch Karolinska Institute; Co-applicant: Prof. M. Narici. 2000-2003.
€315,700 - European Space Agency grant (ESA MESM 15097/01/NL/SH). Co-ordination by Prof. Roberto Merletti, Polytechnic of Torino; Co-applicant: Prof. M. Narici. 2004-2007.

4. Details of the impact

Research has led to impacts on national and international policy decisions relating to space exploration, health benefits for astronauts and people who cannot be physically active. Commercial impacts have also been realised through the development and refinement of new exercise devices.

Impacts on National and International Spaceflight Policy

Since 2005, Narici and Rittweger have acted as expert advisors to various European space programmes. In 2007, Rittweger was appointed to the European Space Agency's Artificial Gravity Expert Group where he continues to contribute to space-based exercise countermeasures. Narici was nominated to the ESA Life Science Working Group Committee in 2007 (until 2013). In 2009, Rittweger was invited to chair ESA's Exercise in Space topical team (until present). Serving as part of ESA's expert panels Rittweger and Narici have contributed directly to the development and definition of ESA's Life Sciences Strategy and work programmes and were involved in the selection of space research applications. The Head of the Directorate of Human Spaceflight and Operation at ESA states, "*The Artificial Gravity Expert Group's work has proven to be very valuable to ESA, and results show that Artificial Gravity has good potential as a space-based countermeasure. This is likely to impact on plans for future space utilisation and exploration, and both Narici and Rittweger have greatly contributed to this success.*" **[A]**

In 2012, MMU Professors Narici and Rittweger were part of the UK Space Agency's advisory committee who contributed to a document in support of the UK Government joining ESA's 'European Life and Physical Sciences Programme (ELIPS) resulting in a £12.4M investment from the UK to exploit insights into the human ageing process http://www.bbc.co.uk/news/science-environment-20421667. Professors Narici was instrumental in organising a dedicated workshop to discuss ELIPS at Kings College London **[B]** as part of the UK Space Biomedicine Consortium (UKSBC). This meeting led to the creation of a document submitted to a ministerial delegation. In

November 2012, the UK government decided to contribute to the 'ELIPS4' programme. As the Co-Ordinator of UKSBC confirms in a full statement available on file **[C],** *"Over the last decade or two there have only been a small number of British people who have been active in space life science R&D to an extent that has impacted the European research scene. Professor Narici and Rittweger are two of the more prominent and successful examples. Quite possibly their heritage aided their ability to tap into the European effort, but also the support and latitude offered by the Manchester Metropolitan University has enabled them to make the impact that they have. The work carried out by MMU was and is recognised at an international level. MMU staff have contributed to hardware and activities on the International Space Station. The UKSBC aim of using space research as a means to benefit terrestrial health care, in particular to combat the effects of ageing. It is through the vision and R&D of founding members such as MMU that this consortium exists and will be able to positively affect the future of a number of sectors of British society. MMU has been a significant factor in the development of this new field of R&D in the UK and will remain at the core of this domain."*

In 2009, Rittweger was appointed to Head of Department at the German Space Agency (DLR). This position has given Rittweger, who retains a 0.2 contract at MMU, an opportunity to direct policy and research strategy at the German Space Agency. It is as a direct result of the influence of his musculoskeletal research that he was appointed to this prestigious and influential role as his Director confirms *"The specific knowledge in musculoskeletal physiology and biomechanics that Dr Rittweger had acquired at Manchester Metropolitan University were the main reasons for head-hunting him for his current position at the DLR institute. The leading position of MMU-based research in this scientific field was well recognized, and given the importance of muscle and bone losses in Space made him an ideal candidate for his position."* **[D].**

Direct Involvement In Space Missions And Associated Clinical Applications

Professor Rittweger's pioneering work in demonstrating the efficacy of vibration exercise as a microgravity countermeasure has led to the wide adoption of this exercise modality for space-related research activities and for physical rehabilitation in clinical conditions. His work has helped to answer questions about how bed-rest studies can help the human body to adapt to living in space. In 2010 the 2nd Berlin Bed-Rest Study http://www.ncbi.nlm.nih.gov/pubmed/20811145 tested the efficacy of whole-body vibration in addition to high-load resistance exercise in preventing bone-loss during bed-rest. A Resistive Vibration Exercise (RVE) evaluated the effect of an intervention protocol on bed-rest induced bone loss. Results showed that retarded bone loss induced by simulated microgravity in humans, when exposed to RVE, was mainly attributed to its anabolic effects. Rittweger's bed-rest work not only aided research in spaceflight but also contributed to significant international clinical advances as evidenced by the Head of the Centre for Child Rehabilitation at the University Hospital Cologne who states, "*these recognitions have been instrumental when conceiving the 'Cologne strategy' for rehabilitation of children with neuromuscular disturbances with various underlying pathologies. Whole body vibration are the main constituents of this strategy…the Queen Rania hospital for prevention and rehabilitation is seeing 300 patients per year and is serving as a role model in Germany and worldwide. Besides the impact of his publications, Dr. Rittweger has also been a continuous source of information for us in joint meetings and collaborations and has substantially contributed." '* **[E]**. This work is having an on-going and direct impact on space missions. For example, in 2012, MEDES, the France-based Institute of Space Medicine and Physiology, carried out the MNX bed-rest study to measure the effectiveness of two counter-measures used against the effects of weightlessness to which astronauts are subjected **[F]**. In order to improve the quality of reports about whole body vibration treatment studies, the International Society of Musculoskeletal and Neuronal Interactions invited experts in the field to provide suggestions on how the intervention should be described in reports. MMU research underpinned these recommendations which were published in 2010 and have impacted on the way in which this work is carried out ever since **[G].**

In 2011, Professor Narici was instrumental in gaining approval from the ESA and NASA to fly the Muscle Atrophy Research and Exercise System (MARES) on-board the International Space Station (ISS). Narici was heavily involved in the conception and design of MARES, which is used by astronauts to prevent musculoskeletal deterioration. Consequently, Narici and colleagues from

MMU (Rittweger **[H]**) and the University of Compiegne were the first to use MARES to support the NASA-approved experiment 'Sarcolab' **[I].** The Sarcolab experiment examined the causes of muscle atrophy and weakness in response to long-term (6 months) spaceflight in 10 astronauts including Dutch astronaut Andre Kuipers who was tested both before and after his mission on the International Space Station. This project represents the first time that astronauts have been tested in this way and will lead to new methods of combating muscle wastage in spaceflight http://www.mmu.ac.uk/news/news-items/1508/

5. Sources to corroborate the impact

[A] Testimonial from the Head of Human Spaceflight and Operations at the European Space Agency corroborating the important and influential role of MMU research / researchers in contributing to ESA spaceflight policy.

[B] Link to proceedings from Kings College London including participation from MMU Professors Narici (who had recently joined *University of Nottingham 2012* p2) Costis Maganaris and Dave Jones (p10, 11): http://www.bis.gov.uk/assets/ukspaceagency/docs/space-science/microgravity-presentations/research-in-space-environments-report.pdf These presentations helped to make the case for UK participation in the European Life and Physical Sciences Programme (ESA)

[C] Testimonial from the Co-ordinator of UK Space Biomedicine Consortium corroborating the long-standing contribution of MMU research to ESA and UKSBC available on file.

[D] Testimonial from the Director of the Institute of Aerospace Medicine at the German Space Agency (DLR) corroborating Rittweger's influence and role and the impact of MMU's research on the decision to appoint him.

[E] Testimonial from the Head of the Centre for Rehabilitation at Centre for Prevention and Rehabilitation of the University Hospital Cologne corroborating international clinical impacts of bed-rest studies

[F] Link to MNX study, MEDES, Toulouse / France, November 2012-end 2013 http://www.medes.fr/home_en/clinical_research/experiments/mnx_study.html corroborating impact of MMU vibration study research on spaceflight and clinical applications.

[G] Link to "Reporting whole-body vibration intervention studies: recommendations of the International Society of Musculoskeletal and Neuronal Interactions" (including a contribution from J Rittweger) evidencing impacts on setting clinical standards and providing guidance in vibration intervention: http://www.ncbi.nlm.nih.gov/pubmed/20811143

[H] DLR web site confirming Joern Rittweger involvement in Sarcolab (paragraph 2): http://www.dlr.de/dlr/presse/en/desktopdefault.aspx/tabid-10172/213_read-7182/year-all/#gallery/10557

[I] Evidence of Prof. Narici's involvement in NASA's 'Sarcolab' experiments (top of page 49): http://www.nasa.gov/pdf/605284main_Expedition_30_31_Press_Kit.pdf

[J] Media coverage of Prof. Narici's involvement in NASA's 'Sarcolab' experiments: http://www.manchestereveningnews.co.uk/news/local-news/manchester-metropolitan-university-boffins-design-874524