Research Assessment Exercise 2020
Impact Case Study

University: The University of Hong Kong
Unit of Assessment (UoA): 15 chemical engineering, biomedical engineering, other technologies (incl. environmental engineering & nautical studies) and marine engineering
Title of case study: Next-Generation Bone Implant Technology for Elderly Patients with Osteoporosis

(1) Summary of the impact

Orthopaedic implants used for fracture repair fail at rates as high as 25% in elderly patients with osteoporosis, primarily due to post-surgical migration. In response, the research team developed two complementary patent-pending technologies:

a. **Soft Implant Tip:** – a novel elastomer tip that reduces implant migration [redacted]

b. **Soft Bone Simulator –** the first particle-based computer simulation of osteoporotic bone, allowing safer implant designs to be developed more rapidly via virtual pre-clinical testing.

The team's spin-out company – **Lifespans, Ltd.** – has subsequently raised [redacted] in private and public funds, completed all testing required for [redacted] next-generation hip implant for the elderly, won numerous local and international awards, joined the inaugural class of [redacted] and in two leading research hospitals in Singapore.

(2) Underpinning research

Osteoporosis affects more than 250 million individuals worldwide. Fractures due to this metabolic disease represent a growing health burden, with 50% of women and 25% of men at risk of injuries in their lifetimes – particularly of the hip, shoulder, and spine. The research underpinning this case study involved the interdisciplinary application of biomechanical engineering theory (the fracture mechanics of porous compressible solid materials) to the problem of reducing the unacceptably high failure rates of orthopaedic implants in the porous, fragile bone tissue of patients with osteoporosis. The research was conducted by an interdisciplinary biomedical engineering team at the University of Hong Kong and their company Lifespans Limited:

Principal Investigator: Professor William W. Lu†	*Dept. of Orthopaedics & Traumatology, 1995 – present; Member of UoA Biomedical Engineering*
Erica Ueda Boles, PhD*	*Former Postdoc under Professor Lu Dept. of Orthopaedics & Traumatology, 2016-17*
Sloan Kulper, PhD‡	*Former PhD Student under Professor Lu Dept. of Orthopaedics & Traumatology, 2013-17*
Co-I: Clinical A/Professor CX Fang†	*Dept. of Orthopaedics & Traumatology, 2010 – present (orthopaedic surgeon)*
Co-I: Clinical Professor FKL Leung†	*Dept. of Orthopaedics & Traumatology, 1996 – present (orthopaedic surgeon)*
Co-I: Professor Alfonso Ngan	*Dept. of Mechanical Engineering, 1993 - present*

** Lifespans Co-Founder/Chief Scientific Officer; † Lifespans Co-Founder; ‡ Lifespans Co-Founder/CEO*

a. **Design of Anti-Migration Implants for Osteoporotic Bone Fracture Repair**

One aspect of the research focused on the development and pre-clinical testing (from 2013-present) of practical implants ready for clinical use as the first application of the novel **Soft Implant Tip** stress-spreading biocompatible elastomer implant tip technology. Underpinning research included publication of novel theories of crack formation in bone-like porous compressible solids in the MIT-run *Journal of the Mechanical Behaviors of Biomedical Materials*

Note: Redaction requested by HKU and accepted by the Engineering Panel

(see Reference [R 1]) in 2018. [redacted]

b. **Fracture Mechanics of Porous Compressible Solids** (e.g. osteoporotic bone tissue)
The second aspect of the research focused on the validation of the theoretical fracture mechanics foundation of the **Soft Bone Simulator** technology through comparisons with empirical findings. The purpose of this research (from 2015-present) was to identify a practical method of predicting implant performance in osteoporotic bone tissue in order to aid in the development of safer and more effective fracture repair implants. This project culminated in the completion of experimental validation studies and its public dissemination in a leading journal of the orthopaedics field – the *Journal of Orthopaedic Research* in 2018 *(see Reference [R 4], presenting the first known application of particle-based modeling of bone tissue to implant migration simulation)*, showing excellent concordance between simulated and experimental results. The results and patents of this underpinning research have led to licensing and commercialization by Lifespans Limited, which is presently engaged in bringing this technology to the market *(see Reference [R 5] for additional underpinning published research related to this project)*.

(3) References to the research

[R 1] Kulper, S.A., Sze, K.Y., Fang, C.X., Ren, X., Guo, M., Schneider, K., Leung, F., **Lu, W.** and Ngan, A., 2018. A novel fracture mechanics model explaining the axial penetration of bone-like porous, compressible solids by various orthopaedic implant tips. *Journal of the mechanical behavior of biomedical materials*, 80, pp.128-136. †

[R 2] Yu, B.S., Zhuang, X.M., Zheng, Z.M., Zhang, J.F., Li, Z.M. and **Lu, W.W.**, 2010. Biomechanical comparison of 4 fixation techniques of sacral pedicle screw in osteoporotic condition. *Clinical Spine Surgery*, 23(6), pp.404-409. †

[R 3] Kulper S, Fang C, **Lu W**, Leung F, Ngan A, Sze K, 2016. A novel fracture mechanics model for osteoporotic bone: enabling the design of safer and more effective orthopaedic implants for elderly patients. *Hip International Journal,* European Hip Congress 2016, Oral presentation OP20-226. †

[R 4] Kulper, S.A., Fang, C.X., Ren, X., Guo, M., Sze, K.Y., Leung, F.K. and **Lu, W.W.**, 2018. Development and initial validation of a novel smoothed - particle hydrodynamics - based simulation model of trabecular bone penetration by metallic implants. *Journal of Orthopaedic Research*, 36(4), pp.1114-1123. ‡

[R 5] Tang, B., Ngan, A.H.W. and **Lu, W.W.**, 2007. An improved method for the measurement of mechanical properties of bone by nanoindentation. *Journal of Materials Science: Materials in Medicine,* 18(9), pp.1875-1881. ‡

† Research supported by Hong Kong ITF Tier 2 grant ITS/171/15FP, entitled *Development of Anti-Cutout Implants for Internal Fixation of Osteoporotic Femoral and Humeral Neck Fractures.* HK$2.2M, 2015-17.

‡ Research supported by Hong Kong ITF Tier 3 grant ITS/470/16, *A Novel Osteoporotic Bone Fracture Simulation System Enabling Safer and More Effective Fracture Fixation Surgery and Implant Design for Elderly Patients*. HK$1.4M, 2017-2019.

(4) Details of the impact

This research has brought benefits to both patients and the broader healthcare industry through

the commercialization activities of Lifespans Limited. This spin-out company has commercialized **significantly safer orthopaedic implants for the elderly** based on the **Soft Implant Tip** *(see Sources [P 1,2], patents invented by the project team and licensed from the University of Hong Kong describing the world's first known instance of a soft elastomeric tip applied to an orthopaedic implant).* These include devices for the repair of osteoporotic fractures in the elderly (proximal femur / hip, and proximal humerus / shoulder) which have been tested for US FDA 510(k) regulatory submission *(see Sources [A 6]),* by Lifespans Limited [redacted] It has also commercialized the **Soft Bone Simulator** *(see Sources [P 3], patent describing the system for predicting implant failure using the world's first known particle-based approach to simulating bone tissue from a CT scan)*, creating a software platform for implant development and surgical planning. For its work on these two technologies, Lifespans has been honored with more than six major awards and competitive grants during the RAE period.

Impact of the **Soft Implant Tip** *[R 1], [R 2], [R 3]*

In comprehensive pre-clinical testing, orthopaedic implants with the **Soft Implant Tip** showed substantial advantages over typical devices and methods used by current market leaders. When applied to a proximal femoral implant and compared to the industry-standard hip screw, the Soft Implant Tip reduced migration rates by up to 25% in synthetic osteoporotic bone tissue under physiologically relevant loading conditions. This finding has been applied to the Lifespan Soft Hip Implant / Dynamic Tip Stabilization System (DTSS), which is presently undergoing final preparations [redacted] Comprehensive pre-clinical safety testing for 510(k) requirements that has been completed and passed with statistically significant results includes:

- *ASTM F384-17 Standard Specifications and Test Methods for Metallic Angled Orthopedic Fracture Fixation Devices;*
- *ISO 10993 Biological evaluation of medical devices (including animal implantation studies meeting or exceeding 13-weeks;*
- *Osteoporotic cadaveric proximal femur biomechanical evaluation* [redacted]

For its work on the Soft Implant Tip, the company received an offer of membership in [redacted] incubator space *(see Sources [A 1] for related press release)*, and the grand prize in international technology competition Hello Tomorrow Singapore, for which the company received a letter of congratulations from the Hong Kong Government *(see Sources [A 2.1] and [A 2.2]),* in addition to several other awards *(see Sources [A 3-5] and [P 1,2]).* Lastly, for the Lifespans Soft Hip Implant / DTSS, the company has secured multiple orthopaedic surgeon partners [redacted]

Impact of the **Soft Bone Simulator** *[R 4], [R 5]*

The results and patents of this underpinning research have led to licensing and commercialization by Lifespans Limited. After attracting the interest of the orthopaedic industry through its partnerships with top manufacturers, Lifespans is engaged in bringing this technology to market as a software platform for rapid validation of safer implant designs. This software has been shown to provide excellent predictive capabilities of implant migration in osteoporotic bone due to bone fragmentation and cracking – a vexing technical problem in the industry for which there is currently no adequate alternative solution. Following successful completion of the ITF ITS/470/16 in 2018, the subsequent commercialization efforts in Lifespans Limited and a joint mainland-HK grant application has attracted interest in research

Note: Redaction requested by HKU and accepted by the Engineering Panel

collaboration and industrial sponsorship from a world-leading orthopaedic devices manufacturer. Akin to the Impact of the Soft Tip technology (see above) this project has contributed to numerous awards and recognition from peers and the greater public conferred to the company *(See Sources [A 1-5] and [P 3])*.

(5) Sources to corroborate the impact

Awards, Articles, and Amici (Letters of Support)

[redacted]

[A 2.1] *Hello Tomorrow 2018 South East Asia Regional Grand Prize* – Winner of a Paris-based international competition focused on deep-technology startups. https://www.versitech hku.hk/news/hku-start-up-wins-top-prize-at-inaugural-hello-tomorrow-singapore-regional-summit

[A 2.2] *Letter of support from the Hong Kong CE Office*– A letter from the Hong Kong CE office was sent to the investigatory team in early 2019, congratulating the team on winning the Hello Tomorrow competition.

[A 3]. *Invention Geneva Silver Medal 2018* - Winner of an international technology prize (for Soft Tip technology), which led to a letter from the HKU Provost Paul Tam. https://www.tto hku.hk/news/the-46th-international-exhibition-of-inventions-of-geneva-april-11-15-2018

[A 4] *Imagine IF! Competition Grand-Prize Winning Technology* – Soft Tip technology was winner of HK finals of Cambridge UK-based international competition focused on biotechnology. https://www.tto.hku hk/news/hku-start-up-wins-championship-at-the-hong-kong-finals-of-the-imagine-if-competition

[A 5] *Hong Kong Technology Startup Support Scheme Grant* – Winner of competitive grants for technology startups in Hong Kong during the years of 2017, 2018, and 2019 to commercialize Soft Tip and Soft Bone Simulator technologies, for a total of over HK$1.7 million in funding. https://www hku.hk/press/news_detail_18162 html

[redacted]

Patents

Patent Family 1: Soft Tip Technology

[P 1.1] Kulper, S. A., Lu, W. W., Leung, F. K. L. & Fang, C.X. Anti-penetration bone implant device and method. US Provisional Patent 62-142,207 (2015); [P 1.2] China PCT patent application (International) PCT/CN2016/078336 (2016); [P 1.3] China Full patent application (National phase) CN107708589A (2017); [P1.4] US Full patent application (National phase) US20180085154A1 (2018); [P1.5] EU Full patent application (WIPO) WO2016155665A1 (2016)

Patent Family 2: Surgical Instrumentation for use with Soft Tip

[P 2] Kulper, S.A., Boles, E.A., Fang, C.X., Leung, F.K.L. and Lu, W.W., University of Hong Kong (HKU), 2019. Surgical extraction device for bone implant tips. U.S. Patent Application 16/032,509. Versitech, Inc. (The University of Hong Kong).

Patent Family 3: Soft Bone Simulator Technology

[P 3.1] Kulper S.A., Ngan A.H., Fang C.X., Guo, M., Lu W.W., Leung F.K.L. Bone model, and modelling process and system therefor. International PCT patent application PCT/CN2017/100889 (2017); [P 3.2] 2019. WIPO Application WO2019047099

Note: Redaction requested by HKU and accepted by the Engineering Panel