Research Assessment Exercise 2020
Impact Case Study

University: The University of Hong Kong (HKU)
Unit of Assessment (UoA): 03 - Clinical Medicine
Title of case study: Novel technology in the treatment of early onset scoliosis

(1) Summary of the impact

Early onset scoliosis is a spinal deformity affecting children which traditionally required repeated surgical distractions. Researchers from The University of Hong Kong developed, optimised and demonstrated the safety and efficacy of a novel magnetically-controlled growing rod (MCGR) which obviate the need for multiple surgeries. This led to a global change of practice, demonstrated by revised international clinical guidelines, FDA approval of the technology (2014) and widespread adoption of MCGR technology. Cost analysis showed usage of MCGR improved healthcare efficiency. The success of this technology led to the acquisition of Ellipse Technologies, the initial MCGR marketer by NuVasive, to develop this technology further.

(2) Underpinning research

Key University of Hong Kong (HKU) Department of Orthopaedics and Traumatology researchers:
Professor Kenneth Cheung (1999-now; currently Head of Department)
Professor Keith Luk (1999-2015, Division of Spine Surgery)
Dr Jason Cheung (2014-now, currently Clinical Associate Professor)
Dr Kenny Kwan (2013-now, currently Clinical Assistant Professor)

Early onset scoliosis (EOS) is a spinal condition in young children which, if left untreated, leads to progression of the spinal deformity, cosmetic disfigurement, poor pulmonary development, and overall poor quality of life. Until 2012, the gold standard surgical treatment for progressive EOS was traditional growing rods implanted under general anaesthesia. This allowed curve control whilst maintaining growth, but repeated surgeries every 6-12 months were required for lengthening, causing morbidities and psychosocial distress. MCGR is a novel technology which, after its surgical implantation, can be distracted by a remote device through the skin in an awake patient. This reduces the number of planned operations and the associated complications. Our research team successfully implanted the first MCGR in a child and published the first case series in the world on its safety and efficacy in 2012 (3.1).

Since then, we have been leaders in researching the optimal treatment protocols (3.2); complications related to the technique of distraction, optimal frequency and amount of distraction per session (3.3); and unplanned reoperations (3.4) in the use of MCGR. Specifically, we reported on the value of a novel distraction protocol in which small frequent distractions to mimic spinal growth are carried out at monthly intervals. We also described novel complications that are specific to MCGR and their incidence. The early experience of our MCGR use led to feedback and discussion with Ellipse Technologies Inc., the developers and manufacturers, regarding improving, optimising and revising the design of the subsequent versions of MCGR. Our research team has been leading international study groups, such as being the Principal Investigator in an international multicentre randomised control trial as part of the Paediatric Spine Study Group (formerly Growing Spine Study Group) in optimising the use of MCGR and identifying risk factors for complications and distraction failure. We have published mid-term results of our own series completing treatment, as well as coordinating and contributing our cases to multicentre studies to report the outcomes and complications of MCGR use. One important and novel finding from these studies is that the "Law of

Diminishing Return"described for traditional growing rods does not occur with MCGR in the same manner, and can be rescued with changing to a new set of implants. This has improved the body of knowledge on treatment of EOS using MCGR.

Radiography has been the accepted method for monitoring distraction and growth in the past. However, the cumulative effects of repeated radiation exposure from a young age may have potential carcinogenic and other harmful effects. Our research team developed a novel non-invasive, radiation-free method using ultrasonography to monitor lengthening during MCGR distraction. Our work has demonstrated the reliability of the use of ultrasonography as an alternative to plain radiographs in visualizing and confirming rod distractions, thereby decreasing their exposure to ionizing radiation and the potential risk of future radiation-induced diseases (3.5, 3.6). This technique is now widely adopted by many centres around the world. By use of ultrasound, radiographs can be reduced to a 6 monthly interval, such that for a 5 year old patient, this technique can reduce over 190 whole spine radiographs by the time of skeletal maturity, significantly reducing their radiation exposure and cancer risk.

(3) References to the research

3.1 Cheung KM, Cheung JP, Samartzis D, et al. Magnetically controlled growing rods for severe spinal curvature in young children: a prospective case series. *Lancet* 2012; 379(9830): 1967-74. DOI: 10.1016/S0140-6736(12)60112-3

3.2 Cheung JP, Bow C, Samartzis D, Kwan K, Cheung KM. Frequent small distractions with a magnetically controlled growing rod for early-onset scoliosis and avoidance of the law of diminishing returns. *J Orthop Surg (Hong Kong)* 2016; 24(3): 332-7. DOI: 10.1177/1602400312

3.3 Cheung JP, Cahill P, Yaszay B, Akbarnia BA, Cheung KM. Special article: Update on the magnetically controlled growing rod: tips and pitfalls. *J Orthop Surg (Hong Kong)* 2015; 23(3): 383-90. DOI: 10.1177/230949901502300327

3.4 Kwan KYH, Alanay A, Yazici M, et al. Unplanned Reoperations in Magnetically Controlled Growing Rod Surgery for Early Onset Scoliosis With a Minimum of Two-Year Follow-Up. *Spine (Phila Pa 1976)* 2017; 42(24): E1410-E1414. DOI: 10.1097/BRS.0000000000002297

3.5 Cheung JPY, Yiu KKL, Bow C, Cheung PWH, Samartzis D, Cheung KMC. Learning Curve in Monitoring Magnetically Controlled Growing Rod Distractions With Ultrasound. *Spine (Phila Pa 1976)* 2017; 42(17): 1289-94. DOI: 10.1097/BRS.0000000000002114

3.6 Stokes OM, O'Donovan EJ, Samartzis D, Bow CH, Luk KD, Cheung KM. Reducing radiation exposure in early-onset scoliosis surgery patients: novel use of ultrasonography to measure lengthening in magnetically-controlled growing rods. *Spine J* 2014; 14(10): 2397-404. DOI: 10.1016/j.spinee.2014.01.039

(4) Details of the impact

Impacts include: health and welfare, economy, commerce

Main beneficiaries include: patients, healthcare providers, industry, international guidelines bodies

Since the first application of MCGR in EOS patients by our research team, and the report of our experience in the *Lancet* in 2012, this new technology has been adopted by spinal surgeons worldwide, leading to a change in clinical practice and guidelines and approval of this technology by the FDA in USA in 2014 [A]. This has had an impact of improvement in patients' quality of life and improved healthcare efficiency. The success of this implant and technology has led to the acquisition of Ellipse Technologies, Inc., the initial marketer of MCGR by NuVasive, Inc. to develop this technology further.

Change in clinical practice worldwide

Although MCGR had been proven safe and effective in large animal studies, its efficacy in humans were unknown. Our research team performed the first MCGR implantation in the world, and subsequently completed the first clinical case series with publication of the results of its short-term follow-up. This important clinical translation and our initial experience of this implant and technology led to a global change in clinical practice and paradigm shift in the surgical treatment of EOS [B]. This is evidenced by the adaptation of this technology, rendering the use of traditional growing rods (TGR) surgeries obsolete in most developed countries [C]. National clinical guidelines for the surgical management of EOS, such as National Institute for Health and Care Excellence (NICE) in the UK in 2014 [Di], Centres for Medicare and Medicaid Services in US [Dii], and international societies, such as the white paper from Scoliosis Research Society [E], and Growing Spine Study Group (GSSG) [F], have included the use of MCGR based on our surgical experience.

Reduction of irradiation exposure of children

The development of ultrasound in the serial monitoring of distractions in EOS patients by our research team has revolutionised the way patients are monitored. The cumulative X-ray dosage from repeated radiography can have potential harmful effects including carcinogenic in later life. The unique features of the MCGR implant that can be captured by ultrasound, as described by our research team, has led to a dramatic decrease in ionising radiation exposure in these children. An independent study showed that this can avoid a mean total effective radiation dose of the pre-lengthening and post-lengthening PA spinal radiographs of 0.26 mSv (range 0.09–0.74 mSv), with the mean attributable lifetime cancer risk of one in 39686 (range 1/89,921–1/9,550) [G]. This technique has also been widely adopted [B].

Improvement in healthcare efficiency

In spite of the high costs of the implant, research teams in the USA, the NICE External Assessment Centre and we have demonstrated that long term reduction in healthcare costs by adopting this technology [Di, H]. It is estimated that MCGR use can generate cost savings of £12,077 per person over a 6-year time period. The decreased use of operating theatres compared with planned reoperations of traditional growing rods and reductions in the associated costs of anaesthesia, nursing, and hospital admissions, have led to improved healthcare efficiency and cost benefits.

Implant sales and continual technology improvement

The success of this novel and innovative technology led to increase in implant sales with a resultant increase in revenue from USD 26m in 2014 to USD 40m in 2015. Eventually, this led to an acquisition of the company by NuVasive, Inc. in January 2016 at USD 380m [Ii]. This allows the implant to be more readily available, and the continual financial benefits and growth in the sales, reaching over USD 1bn for the first time in 2017 [Iii].

(5) Sources to corroborate the impact

[A] 510(k) Number: K140178: MAGEC® Spinal Bracing and Distraction System. FDA, Jan 2014.

[B] Bekmez S, Dede O, Yazici M. Advances in growing rods treatment for early onset scoliosis. *Curr Opin Pediatr* 2017; **29**(1): 87-93. DOI: 10.1097/MOP.0000000000000432 (Ref 38-39)

[C] Keskinen H, Helenius I, Nnadi C, et al. Preliminary comparison of primary and conversion surgery with magnetically controlled growing rods in children with early onset scoliosis. *Eur Spine J* 2016; **25**(10): 3294-300. DOI: 10.1007/s00586-016-4597-y (Ref 12, 16)

[D] National clinical guidelines for the surgical management of EOS:

[**Di**] Jenks M, Craig J, Higgins J, et al. The MAGEC system for spinal lengthening in children with scoliosis: A NICE Medical Technology Guidance. *Appl Health Econ Health Policy* 2014; **12**(6): 587-99. DOI: 10.1007/s40258-014-0127-4 (Ref 3, 7, 13, 19)

[Dii] Centres for Medicare & Medicaid Services [CMS]. Clinical Policy MP354: Growing rods

spinal surgery (2018). ((Page 4, Ref 1, 2, 5, Page 7 Cheung et al 2012, Page 8 Akbarnia et al)

[E] Hardesty CK, Huang RP, El-Hawary R, et al. Early-Onset Scoliosis: Updated Treatment Techniques and Results. Spine Deform. 2018 Jul - Aug;6(4):467-472. https://doi.org/10.1016/j.jspd.2017.12.012 (Ref 22)

[F] Akbarnia BA, Pawelek JB, Cheung KM, et al. Traditional Growing Rods Versus Magnetically Controlled Growing Rods for the Surgical Treatment of Early-Onset Scoliosis: A Case-Matched 2-Year Study. *Spine Deform* 2014; **2**(6): 493-7. DOI: 10.1016/j.jspd.2014.09.050 (Ref 9-10)

[G] Perez Cervera T, Lirola Criado JF, Farrington Rueda DM. Ultrasound control of magnet growing rod distraction in early onset scoliosis. *Rev Esp Cir Ortop Traumatol* 2016; **60**(5): 325-9. DOI: 10.1016/j.recot.2015.01.001 (Ref 5, 10)

[H] Polly DW, Jr., Ackerman SJ, Schneider K, Pawelek JB, Akbarnia BA. Cost analysis of magnetically controlled growing rods compared with traditional growing rods for early-onset scoliosis in the US: an integrated health care delivery system perspective. *Clinicoecon Outcomes Res* 2016; **8**: 457-65. DOI: 10.2147/CEOR.S113633 (Ref 7-8)

[I] Nuvasive Reports:

[**Ii**] NuVasive Pres Release Jan 5, 2016. NuVasive To Acquire Ellipse Technologies.

[**Iii**] NuVasive Inc. 2017 Annual Report.