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EDITORIAL

Transcutaneous osseointegration for amputees

LESSONS FROM THE PAST OF RELEVANCE TO THE FUTURE

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Transcutaneous limb osseointegration improves pain, mobility, and quality of life for patients struggling with a traditional socket prosthesis (TSP)[1,2] by eliminating the socket and anchoring the prosthetic limb to the skeleton. This represents the greatest paradigm shift in amputee rehabilitation since Ambroise Paré's prosthetic designs in the 1500s.[3] Given the recent USA Food and Drug Administration (FDA) approval of, and large government-sponsored organizational interest in osseointegration implants,[4,5] a surge of implant development and surgical interest is forthcoming. Understanding the origins and evolution of osseointegration, including the unsuccessful attempts, is both interesting and clinically responsible to help enterprising surgeons and implant manufacturers avoid known design and technique shortcomings. Repeating known problems increases development time and cost and causes patient morbidity, while evoking unwarranted disapproval from the medical community.[6] Accordingly, this editorial has two aims: first, to inspire and guide interested perusal of early foundational literature, which unfortunately is sometimes difficult to locate or even identify; and second, to call for more responsible reporting of situations which lead to patient morbidity.

The first osseointegration attempts were performed by G. Dümmer in 1946, a general surgeon from Pinneberg, Germany.[7] He inserted a stainless steel rod with a cross-locking screw into four transtibial amputees. All required removal after a brief period, presumably due to loosening and infection. Between 1956 and 1969, John Esslinger with the USA Veterans Administration (VA) performed animal experiments using stainless steel, titanium, Teflon, and rubber implants anchored to the bone via metal meshes.[8] Contemporaneously, Vert Mooney at Rancho Los Amigos attempted osseointegration in humans with two different implant styles: porous ceramic implants with direct bone contact,[9] and intramedullary cementation of stainless steel rods, similar to total joints.[10] Unfortunately, none of these designs and techniques achieved long term stability.

The discovery of an entirely new biological phenomenon was critical in addressing implant loosening. Several researchers between the 1940s and 1960s observed that bone strongly integrated directly with titanium implants without inflammation.[11–15] By 1965, Brånemark et al[16] proved titanium could maintain solid dental implant fixation for many years, eventually coining the term 'osseointegration', which now refers both to the biological phenomenon as well as the surgical technique for amputees. Osseointegration research quickly identified important material-biological properties. In 1971, Galante et al[17] demonstrated bone interdigitated into titanium implant surfaces > 300 µm by seven to ten days, and achieved maximum pull-out strength of 20 kg/cm^2 by two weeks. In 1972, Predecki et al[18] reported bone deposited fastest in 500 µm to 1,000 µm channels and ingrowth required surface roughness > 20 µm: larger diameter channels take longer due to increased vasculature required to metabolically support the bone; < 95 µm was prohibitive of osseointegration. In optimized conditions, osteocytes form tight junctions with titanium featuring hemidesmosome anchorages.[19] In contrast, fibrous tissue inevitably develops between bone and cement or stainless steel, with no direct bone ingrowth or ongrowth. These

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studies established titanium as an excellent osseointegration material.

Despite the resounding success of dental osseointegration and improved material-biological science knowledge, clinically successful limb osseointegration remained a generation away. From 1967 to 1985, Charles William Hall, also commissioned by the VA, organized a series of experiments with the goal of making amputee osseointegration a reality. The complete list of his work is itself published and is essential reading for anyone seeking to innovate implant designs or surgical techniques,[20] and includes all the subsequently mentioned studies. Hall, who helped William Debakey develop the artificial heart, initially had three goals for osseointegrated prostheses: they should be a permanent weightbearing skeletal extension, the patient should be able to directly control distal joints on an external prostheses, and the implant should have a natural appearance. Hall initially thought that bone could not withstand direct impact from a prosthesis and included shock absorption mechanisms, but found that chemical breakdown eventually occurred between implant interfaces. Shock absorbers were proven unnecessary when updated implants excluding them did not cause fractures. Hall initially moved external prosthetic joints via artificial tendons sewn to remnant tendons and passed transcutaneously to attach to the articulating prosthesis. Infection problems led to this goal's eventual abandonment.

Some of Hall's paramount discoveries concern the skin-implant interface and infection. He steadfastly believed that skin-implant seals against bacterial ingress were imperative, and tried using fabrics including Nylon velour. These constructs failed because of what Hall called the "growth phenomenon". Basal cells permanently bonded to the fabric, and upon maturing and migrating superficially to become the stratum corneum, they inevitably also pulled the implants out. Another skin-related obstacle Hall identified was the "wedge effect": dead skin cells must be cleared away or else they accumulate as a wedge between the implant and the living skin. Hall also recognized that epidermal epithelial cells grow until all cells achieve circumferential epithelial cell contact. When implants interrupt epithelial continuity, the skin tends to form deep tunnels or marsupialize the implant. Like Malgaigne[21] before him, Hall recognized that skin movement and tension in multiple planes precipitates irritation, inflammation, and infection. Deserving specific mention, in 1974 Hall et al[22] iterated that the bone must outpace bacteria in a "race to the implant", more than a decade before Gristina et al[23] popularized the concept. If bacteria reach the implant before host tissue integrates, infection is inevitable. Hall concluded experiments in 1985, never attempting human osseointegration.

The history of osseointegration following Hall is discussed extensively in recent reviews,[24] so only the briefest highlights will be reiterated. Three major osseointegration implants are currently available. In 1990, Rickard Brånemark — Brånemark's son — performed the world's first long-term successful osseointegration for a human amputee using the Osseointegrated Prostheses for the Rehabilitation of Amputees (OPRA), a titanium screw which threads into the skeletal residuum at an initial surgery, to which a transcutaneous prosthesis is attached at a second surgery.[25] Horst Aschoff designed a cobalt-chrome press-fit implant in 1999 (first named Endo-Exo, renamed Integral Limb Prosthesis, ILP), also recommending two surgical stages.[26] Design modifications concerned skin interface problems. Munjed Al Muderis designed a press-fit titanium implant in 2013 (Osseointegrated Prosthetic Limb, OPL) and currently advocates only one surgical stage.[27] Al Muderis has published articles describing osseointegration success in diabetic[28] and dysvascular amputees,[29] and oft-neglected anatomical locations.[30,31] Three implant designs have been recently investigated but are not commercially available. The Intraosseous Transcutaneous Amputation Prosthesis (ITAP) featured hydroxyapatite coating to promote a permanent skin-implant seal against bacteria, but trials ended due to frequent infection. The researchers stated that the implant company has legally impounded the data.[32,33] The Percutaneous Osseointegrated Prosthesis (POP) aimed to achieve osseointegration only at a small surface and had multiple modifications over the last decade, but loosening remains common, and the apparently concluded trial[34] results are unreported. Recent interlocking screw designs,[35] reminiscent of Dümmer's 1946 concepts,[7] seem directed at trying to address that problem. A modified Compress tumour prosthesis which provides continuous compression has been under continuous investigation since 2017 with only minimal early reporting available.[36]

It is an exciting time for osseointegration. Amputees typically achieve better mobility and quality of life,[1,2] permitting careful experiments to expand care to patients with conditions previously considered contraindicated.[28–31,37] However, classic challenges still require thoughtful attention: while periprosthetic fracture seems manageable,[38] infection remains problematic.[39] Amputee osseointegration is entering an era of rapid innovation and experimentation, so it is critical that we adhere to the quintessentials: innovation guided by the fundamentals of our predecessors, and likewise reporting misadventures without commercial sequestration of data,[33] lest we repeat blunders. Cementing transcutaneous osseointegration implants is an obvious example: as Mooney et al[9,10] reported in the 1970s, this approach fails; when ITAP trials confirmed this, the failure data were withheld,[33] leading to a third generation committing the same error.[40] Awareness of and access to foundational knowledge, along with timely reporting of newly discovered problematic situations, could have prevented this patient's and potentially future patients' morbidity, because it is patients — not the surgeons or implant companies — who suffer the consequences of poor clinical outcomes. Recounting lessons is better than recalling implants.[6]

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