TITLE PAGE

Title
Bone reconstruction: a history of vascularised bone transfer

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Running Title:
On the history of vascularised bone transfer

Presentation:
This paper was presented in part at the Royal Australian College of Surgeons Annual Scientific Conference on May 2⁰, 2015 in Perth, Australia.

Keywords:
Vascularised bone transfer; bone reconstruction; history.
Defects of bone have captured the imagination of reconstructive surgeons for millennia\(^1\). The earliest attempts at bone reconstruction date back to 2000 BCE when Peruvian priests implanted metallic plates to reconstruct the contour defects of religious trephination\(^2\). Calvarial defects remained the focus of bone reconstruction for some time. In 1668, Jobs van Meekeren reported the use of dog bone graft by a Russian surgeon to reconstruct the calvarium in a soldier\(^3\). The graft healed too well, and the man was subsequently ostracized from his religious community because of the perceived impurity of the xenograft. Experimentation with non-vascularised bone graft, both autologous and allogeneic, followed throughout the 19\(^{th}\) century until it was fully appreciated that preservation of a blood supply to bone prevented resorption and improved the likelihood of bone healing\(^4\). And so the scene was set, as surgeons, biologists and immunologists recognized that in order to preserve the structural integrity of bone, it should retain a blood supply and be harvested from an autologous source\(^5\).

Autologous vascularised bone transfer has since evolved in parallel with other advances in reconstructive surgery including bone handling, fixation and microsurgery\(^6,7\) leading to the higher rates of union\(^8,9\), resistance to resorption\(^10,11\) and biomechanically superior outcomes\(^9\) that are enjoyed today, even in the setting of complex defects\(^12\).

Our aim is to reflect on the evolution of vascularised bone transfer, its key pioneers, the changing indications for its use and progress in understanding the patterns of blood supply to bone.

**EARLY HISTORY OF BONE BLOOD SUPPLY**

In a letter to the publisher *Philosophical Transactions* in 1674, Antoni van Leeuwenhoek first described what would become known as the Haversian canal. Clopton Havers would later formally describe this system and surmise its role in providing nutrients to the surrounding bone lamellae. He communicated his famous work, the so-called “Osteologia Nova”, to the Royal Society in 1691\(^13\). Bernhard Albinus, considered by many to be an expert of dissection in the 18\(^{th}\) century, expanded on the work of Havers and van Leeuwenhoek and was the first to fully appreciate the finer vasculature within bone\(^14\). With the aide of microscopy, he would describe the periosteal
and medullary origins to bone. Despite these findings, bone appeared to be considered a relatively inert tissue by many for the purposes of osseous reconstruction throughout most of the 19th century.

NON-VASCULARISED BONE GRAFTS

Phillips von Walter described the first clinical use of non-vascularised bone autograft for the reconstruction of a calvarial trephination defect in 1820. The advent of general anaesthesia, thanks to William Morton and others in 1846, paved the way for more daring and aggressive surgical experimentation. Tibial non-union and osteomyelitis remained a common indication for surgical resection during this time, and although the value of preserving the periosteum was appreciated by pioneers such as Ollier, highly variable results were attained with non-vascularised bone grafting during this time period. Barth, an orthopaedic surgeon from Germany, discussed "schleichenden ersatz", that is, the absorption of necrotic bone and its slow replacement by the growth of new bone from the surrounding living osseous tissue. The American surgeon Curtis reported similar observations around the same time as Barth, unknown to either of them. This process would later appropriately become known as "creeping substitution" by Phemister—a concept that is now fundamental to modern day bone tissue engineering. Curtis would go further at this time and went on to describe the importance of preserving the blood supply to bone, and thus its vitality to ensure healing without the inherent risk of resorption.

"...the ideal of the future: the insertion of a piece of living bone which will exactly fill the gap and will continue to live without absorption."

PEDICLED VASCULARISED BONE TRANSFERS

Building on the concept of ensuring bone vitality to ward off graft resorption, the German surgeon Wilhelm Wagner (1848-1900) likely performed the first vascularised bone transfer based on a regional pedicle with a soft tissue carrier for a calvarial defect in 1889. His so-called "osteoplastic flap" (Figure 1) permitted him surgical access to the cranial vault without the problem of a residual calvarial defect by using only the outer table of calvarium attached to...
a soft tissue paddle\textsuperscript{20}. Reportedly, he had minimal complications with bone resorption and the approach would later become a standardized method for access to the brain, popularised by pioneers in neurosurgery such as Harvey Cushing. Shortly after this in 1892, another German surgeon, Bardenheuer (1839-1913), would describe a pedicled flap of the central mandible for an ipsilateral segmental mandibular defect, preserving soft tissue attachments in the process\textsuperscript{21}.

Throughout the late 19\textsuperscript{th} century, vascularised bone transfer was largely borne out of the need to replace long en-bloc segments of bone where non-vascularised bone graft had already failed. In the limbs, these patients would often be subjected to amputation, with rates of perioperative mortality during this time as high as 70\%\textsuperscript{1}. However, in 1891 the former president of the American Orthopedic Association Abel M. Phelps (1828-1912) experimented with a xenograft from a dog in an effort to avoid amputating the limb of a young boy with tibial non-union\textsuperscript{22}. Both the canine donor and human host remained attached to each other for nearly two weeks, with the xenograft bone vascularised by the canine nutrient artery. This early attempt at transplantation was cut short due to illness in the dog (likely the early signs of acute rejection), although not before Phelps claimed to have identified some early signs of bony union.

Pedicled bone transfers emerged as an alternative for bone defects that did not heal with non-vascularised bone grafts throughout the early to mid 20\textsuperscript{th} century. In 1904 Nichols was the first to report success with the pedicled fibula flap, using it for ipsilateral reconstruction in a series of patients with tibial non-unions and chronic osteomyelitis\textsuperscript{23}. This was the first true regional bone flap reported in the literature and was subsequently popularized by Huntington (1849-1929) in his famous orthopaedic work “Case of bone transference. Use of a segment of fibula to supply a defect in the tibia” in 1905\textsuperscript{24} (Figure 2).

**BONE TRANSFER BY PRELAMINATION**

World War I brought with it many opportunities for facial reconstruction, particularly of inter-calary defects of the mandible following blast injuries. Vilray P. Blair (1871-1955), an American war-time surgeon, made early use of
both the *delay concept* and *creeping substitution* to prelaminate rib autograft in a supraclavicular skin flap for extended mandible reconstruction in 1915 (Figure 3). His results were published in his well known treatise “*Surgery and diseases of the mouth and jaws; a practical treatise on the diseases of the mouth and allied structures***”. Others around this time also reported the use of delayed regional options for bony reconstruction in mandibulofacial defects such the German plastic surgeon Erich Lexer (1867-1937). However, the practical hindrances of prelamination and pedicled bone grafts limited their translation into routine reconstructive surgery with their applicability limited to specific anatomical sites and clinical circumstances where the zone of injury was narrow. Therefore, during the early part of the 20th century, non-vascularised bone was considered suitable for most defects by surgeons of the day and could be transferred easily as a graft to the defect site. The establishment of antiseptic practices throughout the early 20th century, originally pioneered by Lister, and the emergence of penicillin would support a growing dependence on non-vascularised bone by reconstructive surgeons like Millard and others.

**NEW CONCEPTS IN BONE BLOOD SUPPLY**

It was not until the early and middle 20th century that modern investigators concerned themselves with the questions concerning the pattern and behaviour of bone blood supply as it applied to musculoskeletal pathology, such as osteoporosis and fracture healing. This work on bone blood supply would later prove crucial to the design and application of free vascularised bone transfer. Joseph Trueta (1897-1977), a former Professor Emeritus of Orthopaedic surgery at Oxford, worked extensively on describing the pattern of cortical bone blood flow in both lower mammals and human cadavers. He found that the inner two-thirds of the cortex in long bones was predominantly vascularised by the medullary circulation, with the outer one-third supplied by the periosteal system. Henry “Harry” V. Crock (b. 1929), a great Australian orthopaedic and spinal surgeon, made important contributions to our understanding of bone blood supply and extended much of the work of Trueta, who was a great mentor for him during his time in England. Crock worked predominantly with cadaveric tissues and mapped...
the blood supply to the various key anatomical sites such as the proximal femur, knee and spine; he also validated Trueta’s work, finding a significant contribution of the periosteal blood supply to cortical bone and defining anastomotic connections between the endosteal and periosteal circulations\textsuperscript{29}.

The British physician Murray Brookes (b. 1926), challenged the views espoused by Trueta and Crock with his own experiments in both rabbits and cadavers, suggesting a predominant blood supply to the diaphyseal cortex from the endosteal system\textsuperscript{30}. He further expanded on this concept and identified that the blood supply from these two systems was dynamic during life, with a progression towards a dominant blood supply in the diaphysis of long bones from the periosteal circulation in later life\textsuperscript{31}. Around the same time as Brookes, Frederich Rhinelander (1906-1990) investigated the blood supply to long bones in setting of fracture healing, osteotomy and internal fixation\textsuperscript{32}. Using lower mammals, he revealed the potential pitfalls in using intramedullary fixation where the endosteal blood supply is inherently interrupted by a tight fitting Künstcher nail. In this setting, the periosteal blood supply is found to take dominance with regard to cortical bone vascularity once the endosteal supply is interrupted – a concept that would later be used to support the use of vascularised bone transfer of the rib, scapula and radius for mandible reconstruction\textsuperscript{5}.

MICROSURGERY AND FREE VASCULARISED BONE TRANSFER

Following the introduction of the microscope into reconstructive surgery by Jacobson\textsuperscript{33} and the successful auto-transplantation of free vascularised tissue throughout the early 1970s\textsuperscript{34,35}, intensive investigation was also underway to determine the feasibility of free osseous tissue transfer. Early experimental work\textsuperscript{6} led to an increased appreciation for not only the surgical underpinnings but also the potential biological advantages in using vascularised osseous tissue for bone reconstruction. Using the concepts of bone blood supply espoused by those before them\textsuperscript{28-30,32}, Ostrüpp and Frederikson were the first to experiment with free vascularised bone transfer\textsuperscript{6}. In a canine model, they established the feasibility of free vascularised rib transfer for the reconstruction of the mandible. Discussion concerning the viability of bone from different donor sites grew, and Berggren evaluated the
role of the periosteal and medullary circulations on rib transfer in dogs — experimenting on the disagreement between Trueta and Brookes. He found that rib viability could be retained with revascularisation on the periosteal circulation alone and that no difference in bone healing was identified when compared against vascularised bone based on both the medullary and periosteal circulations.

Andrew J. Weiland and coworkers would later help to establish the role of vascularised bone in providing a greater healing potential compared with non-vascularised bone grafts in their article titled “Bone grafts: a radiologic, histologic and biomechanical model comparing autografts, allografts and free vascularised bone grafts.” With greater rates of union, resistance to resorption and biomechanically superior outcomes in conjunction with the ability to transfer bone to any desired location, free vascularised bone transfer would emerge as an attractive option. The preceding centuries of work would culminate in Taylor performing the first successful vascularised bone transfer using a free fibula flap on June 1st, 1974 to reconstruct a 12.5cm intercalary defect of the lower tibia from a motorbike accident. At 40 years follow up, hypertrophy of the fibula flap is clearly present and excellent bony union is established, with full mobility of the limb achieved (Figure 4). Following this report, the free fibula flap emerged as a workhorse option for free tissue transfer in the setting of major bone defects, especially of the long bone and mandible. Other anatomical locations exploited for the purpose of free bone transfer expanded and included the iliac crest, scapula, radius and more recently the medial femoral condyle. Many of these flaps continue to be used today for a range of defects, particularly the craniofacial skeleton after tumor ablation and the long bones following trauma, infection and malignancy.

EMERGING ROLES FOR VASCULARISED BONE TRANSFER

Novel modes of bone reconstruction are emerging and the role of vascularised bone transfer appears to have evolved alongside these developments (Figure 5). Tissue engineering is providing tailored methods of bone reconstruction with the use of prelaminated osseous flaps. In 2004, Warnke described the use of a 3-D printed, prelaminated scaffold buried in
the latissimus dorsi for a delayed reconstruction of a large central mandibular defect (Figure 6). Recent work is also underway which integrates the use of vascularised bone transfer and scaffold biomaterials to reconstruct critical sized long bone defects in a large animal experimental model. Following some success with vascularised bone allo-transplantation for bone defects in the 1990s, attention is now turning to use of vascularised bone in composite defects as part of a Vascularised Composite Allotransplantation (VCA) reconstruction. The use of whole bone and requisite soft tissue permits a highly accurate and anatomical reconstruction for a given defect. Furthermore, the inclusion of vascularised bone marrow in the allograft presents as an exciting development to help induce donor-specific tolerance with mixed chimerism.

Free vascularised bone transfer has evolved to become an accepted and often the preferred reconstruction for critical size bone defects in both the axial and appendicular skeleton. A review of its history shows a stepwise evolution in the complexity of vascularised bone grafts, that, following the recognition of blood supply preservation in healing, has matched the reconstructive indications at respective time points in history.
REFERENCES


3. van Meekeren J. Observationes Medico-Chirurgicae. Amsterdam: Ex Officina Henrici & Vidnae Theodori Boom; 1682.


FIGURE LEGENDS

Figure 1 – Schematic from *Chirurgie Opératoire du Système Nerveux* by Antony Chipault\(^\text{20}\) describing his experience with Wagner’s “osteoplastic flap” technique.

Figure 2 – Series of x-rays (A, B) and photographs (C) by Huntington in 1905\(^\text{24}\) demonstrating bony reconstruction of the tibia with the pedicled fibula flap. This approach was inherently reserved for difficult and recalcitrant non-unions as well as osteomyelitis.

Figure 3 – Portrait of Vilray P. Blair (1871-1955) (A) and illustrations (B, C) from his work on mandibular reconstruction with pre-laminated bone flaps\(^\text{25}\). Portrait courtesy of Visual Collections of the Becker Medical Library, Washington University School of Medicine.

Figure 4 – This series of x-rays show the progressive healing of the first successful clinical free vascularized bone flap transfer to reconstruct a traumatic 12.5-cm defect of the tibia. (A) The fibular free flap with a patent vascular anastomosis 6 weeks after surgery (arrow). (B) Bony union of an undetected traumatic fracture at nine months follow up (arrow). (C) rapid hypertrophic union of the fibula over the next three months and (D) segmental bone defect healing at 40 years follow up. Reproduced with permission from Taylor *et al.*, 2016\(^\text{12}\)

Figure 5 – Timeline illustrating the evolution of vascularised bone transfer over the last few centuries. Key figures reproduced from respective sources\(^\text{6,7,20,24,25,33}\), with permission where appropriate. Portrait of Abel M Phelps courtesy of The Lillian and Clarence de la Chapelle Medical Archives at NYU.

Figure 6 – (A) Three dimensional CT scan of a near total mandibular defect reconstructed with a tissue engineered prelaminated bone flap. (B) Skeletal
scintography confirming bone remodeling and mineralization. Reproduced with permission from Warnke et al., 2004\textsuperscript{36}.
Figure 2

274x155mm (72 x 72 DPI)
Figure 3

278x116mm (72 x 72 DPI)
Figure 4

423x324mm (72 x 72 DPI)
Figure 5

346x245mm (72 x 72 DPI)
Figure 6

241x120mm (72 x 72 DPI)