Osteosarcoma is the most common primary bone tumor of the appendicular skeleton, frequently affecting large breed dogs. While amputation is considered the gold standard for removing the tumor, many owners would prefer a limb-salvage technique and some dogs are not suitable candidates for amputation given comorbidities such as neurologic disease, obesity, or debilitating osteoarthritis. Therefore these techniques are increasingly employed. The objective is to enable complete resection of the malignancy and restore pain free limb function. Techniques include longitudinal bone transport, microvascular anastomosis of bone transplant, bone transposition (ulna for radius), cortical allografts, endoprostheses, extracorporeal intraoperative radiation therapy and autograft pasteurization. Metallic endoprostheses may be technically easier to apply than allografts and do not rely on bone harvesting and banking. Other recently available options for pain palliation and short-term provision of functional limb use include stereotactic radiation therapy and plating of osteosarcoma-affected bone.

Preoperative skeletal imaging for all cases includes orthogonal plane radiography, computed tomography and magnetic resonance imaging of affected limbs. Diagnosis may be additionally refined using pre-operative cytology, histopathology and appropriate staging for local or distant metastases. In the UK, neoplasia is overwhelmingly the most common cause of destructive osseous lesions with variable periosteal proliferation, since fungal and other neoplasia-mimicking osteomyelites are rare. Therefore frequently full-mass resection is preferred to staged biopsy in the interests of timely intervention. Radiographic and CT-scan documented absence of grossly discernable pulmonary metastatic disease is a prerequisite for limb salvage and adjuvant chemotherapy protocols are considered fundamental to standard of care.

Limb salvage techniques have been most commonly employed for malignancies of the distal radius. Clinical outcomes at this site are often positive, with minimal compromise of limb function by pancarpal arthrodesis. To date simple metallic spacers with a single plate anchored to the proximal radius and a single metacarpal bone have been employed. Limb spare application at other sites including distal femur, distal and proximal tibia, proximal humerus and proximal femur have been associated with more variable outcomes.

There have been limited reports of the usage of endoprosthesis for limb-sparing surgery in veterinary medicine. A biomechanical study showed superior axial strength of endoprosthesis limb-sparing surgery when compared with cortical allograft replacement. A clinical case series using a 316L stainless steel commercially available endoprosthesis showed that this could be used satisfactorily for limb-sparing surgery and there is one report of a custom tantalum implant with a good outcome. Interestingly, infection has been correlated with increased median survival times, but results in management issues.

We have employed titanium and stainless steel modular endoprostheses with customized honeycomb collars and intramedullary pegs coated with hydroxyapatite to facilitate osseous ingrowth in addition to stainless steel peg-cemented implants at multiple sites, including arthrodesis of the carpus and hock and including a hinged knee joint for the distal femur and proximal tibia. The relative advantages of HA-coated versus cemented intramedullary stems have not been elucidated to date, and the advantage may best be realized with less rapidly terminal pathologies such as chondrosarcoma or osteoblastoma, where implant-bone construct resilience may be required for several years.
As endoprostheses for the treatment of osteosarcoma becomes more popular, increased availability of implants, ideal implant structure, and implant material selection will influence overall patient outcome. Presently an excellent quality of life can be provided – with the caveat that survival time is limited by metastases for all cases and local recurrence for a small number of cases. The time of intervention relative to the time of diagnosis has a major influence on survival time, but the median is approximately 11 months. The author wishes to encourage all primary care clinicians to discuss euthanasia, full limb amputation and limb spare on the day of diagnosis and refer for limb spare as soon as possible if the owner wants to explore this possibility, since time is absolutely of the essence.

Consistent weight-bearing limb can be achieved by 1 week post-operatively for most cases. Veterinary and owner assessment generally perceives resolution of pain by 1 week postoperatively. Radiographic reassessment has revealed implant integrity without periprosthetic osteolysis from 12 weeks to two years at least and owners tend toward universal satisfaction, though the first few weeks postoperatively are difficult emotionally and practically. The level of functional restoration is dramatic with most patients returning to full range exercise.

For radial and ulnar endoprostheses, novel application of an ulnar linkage plate (to the proximal extent of the olecranon) and two rather than one metacarpal plates may assist early mobilization and promote resilient biomechanical function. The modular implant design has putative advantages by comparison with existing endoprostheses by distributing load to all available osseous segments, allowing unrestrained intramedullary implantation and prosthesis attachment, precise functional limb axis alignment and optimization of available bone stock in both proximal and distal segments. This may be particularly pertinent to the antebrachium where elbow disease as a result of iatrogenic incongruency or malalignment may contribute to poor outcome and where pronation-supination may contribute to implant loosening.

Recently, combination of synthetic and metallic mesh layering techniques have been successfully employed for attachment of proximal limb musculature to a custom manufactured total hip replacement implant construct for limb salvage treatment of proximal femoral osteosarcoma. This heralds the possibility of custom joint replacement at other anatomic sites.

2 ENDOPROSTHESES WITH ATTACHED EXOPROSTHESES
- Intraosseous Transcutaneous Amputation Prosthesis (ITAP)

Full-limb amputation frequently constitutes the standard of care for appendicular neoplasia and irreversible vascular or neurological compromise in both human and canine patients. The author concurs that full-limb amputation is appropriate and indeed the best option for resolution of pain and restoration of quality of life in many cats and dogs. Amputation of a single limb results in an adequate functional outcome and good level of owner satisfaction in most cases. However, there are circumstances where euthanasia or limb salvage may be the only reasonable options, for example in chondrodystrophic breeds that may not have adequate function on three legs, giant breeds of heavy bodyweight with multi-articular multi-limb osteoarthritis, severely obese animals, animals with double limb amputation after traumatic events or patients affected by neurological dysfunction. It is for these cases that limb prostheses may be considered. The author does not condone or recommend application of prostheses unless there are substantial physiological reasons to do so and the procedure can be deemed ethically and morally sound. Anticipated lifestyle (and corresponding owner expectations) should also be considered, with amputation being less readily accepted by very active, performance or working animals. Increasingly, animal owners are actively requesting consideration of this option.
In veterinary surgery indications for full limb amputation include severe trauma, ischemic necrosis, intractable orthopaedic infections, unmanageable arthritis, paralysis, congenital deformity or neoplasia. Precise incidence and epidemiological data for small animal amputations have not been reported. Recent investigation has reported changes in ground reaction forces in large breed dogs following limb amputation. It has been reported that dogs with thoracic limb amputations have more difficulty keeping their balance, and fall more often, whereas dogs with pelvic limb amputations have more difficulty in gaining speed, especially during the initial post-operative period. These findings have been corroborated by a recent publication that documented significant changes in force plate analysis following both thoracic and pelvic limb amputations. Gait changes are considered greater following thoracic limb amputation than pelvic limb amputation.

Osteosarcoma (OSA) is the most prevalent canine primary bone tumor and reported methods of managing this cancer include palliative care, radiation therapy, chemotherapy, radical surgical excision, limb sparing procedures or a combination thereof. Limb amputation or limb-salvage strategies aim to eliminate local disease but metastases occur in most cases regardless of treatment protocol. According to the National Canine Cancer Foundation an estimated 6,000-8,000 new cases of canine osteosarcoma (OSA) per year are identified in the US alone representing a significant therapeutic challenge to the veterinary community. Other appendicular malignancies especially those involving joints such as synovial cell sarcoma present a similar therapeutic challenge, albeit that prognosis regarding longevity post-excision may be superior to OSA. Tumours involving the carpus and/or metacarpus may also represent a significant therapeutic challenge, with treatment options including palliative care, radiation therapy, chemotherapy and limb amputation. Distal limb trauma is another common cause for amputation and where irreparable vascular and neurogenic trauma has occurred, partial or full amputation may be the only realistic option.

Stump socket prostheses (SSPs) applied following partial limb amputation are common in human medicine and are available commercially for the veterinary market. Sporadic reports detailing SSP application in dogs have appeared within the veterinary literature following a pioneering report detailing application by Hobday in 1906. Currently, SSP designs rely on the stump-socket interface for attachment and transmission of load-bearing forces from the prosthesis to the load bearing bone and soft tissues. In humans this leads to frequent problems including skin rubbing, infection and tissue necrosis particularly prior to acclimatization of the stump. Such exoprosthesis typically require custom manufacture and regular refitting or adjustment, may be difficult and uncomfortable to maintain, and experiences within the small animal veterinary field have sometimes been disappointing – either because of poorly manufactured or fitted devices or because of poor owner or patient compliance. Recently significant advances have been made by groups in the UK and USA, where experience of successfully fitted SSPs has been gained in dogs with different levels of amputation in both the thoracic and pelvic limbs.

Direct osseous and dermal integration of an implant provides an opportunity to alleviate the need for weight bearing at the skin socket interface. In contrast, loading is transferred from the exoprosthesis to a long-bone at the level of amputation by means of an implant that is anchored within the bone. Intra-osseous and transcutaneous prostheses have been development since the 1960s in the human surgical field. Initial applications included cosmetic dental and aural prostheses. Subsequent attempts to translate this technology as a means of attaching exoprosthesis to limb stumps of amputees have been limited by skin complications including infection, epithelial down growth, marsupialization and periprosthetic soft tissue necrosis. The recently developed Intraosseous Transcutaneous Amputation Prosthesis (ITAP) successfully applies ultrastructural geometry gleaned from a natural biomimetic model, the deer antler, to create a soft tissue-implant interface which acts
as a barrier to exogenous agents, and in particular may prevent down growth and marsupilization. The background and bench research involved in ITAP development was achieved at University College London by Prof Gordon Blunn and Dr Catherine Pendegrass.

The author considered purported advantages of ITAP would be of potential benefit to selected dogs with disease of the distal limb. Only a single peer-reviewed report previously described successful fabrication, surgical preparation and implantation of transcutaneous tibial implants in a dog that suffered malicious bilateral partial pelvic limb amputation. Despite aseptic loosening of one implant requiring revision surgery at 14 months and challenges with skin retraction along the implant surface (porous titanium), long term clinical outcome was positive. The author has applied ITAP to distal thoracic and pelvic limbs of canine patients following traumatic and neoplastic injury with encouraging results for the past five years. Of interest, our early case series represented the first application of ITAP to a weight-bearing limb segment in any species. Subsequent to these cases, and applying techniques evolved and knowledge derived from implantation of these patients, ITAP was successfully applied to the humerus and femur of human patients – a good example of application of translational findings for the benefit of both species. More recently in animals, ITAP has been applied to the calcaneus with talo-calcaneal fusion to produce a “foot” for the pelvic limb of a dog and both pelvic limbs of a cat.

The device functioning as a distal limb prosthesis consists of two subunits, the ITAP (endoprosthesis) linking the distal limb with a weight bearing attachment (exoprosthesis) for transfer of ground reaction forces. The ITAP device was developed by the Centre for Biomedical Engineering at the Institute of Orthopaedics of University College London under the auspices of Stanmore Implants Worldwide. The ITAP has multiple functions: a dual biological function to promote osseous and dermal integration at the limb-implant interface thereby achieving a permanent biological seal; and a mechanical function of coupling of the limb to the exoprosthesis. The ITAP consists of three subunits, a shaft to promote osseous integration, a flange to promote dermal integration and a distally protruding peg allowing connection to an exoprosthesis. Each subunit had specialized biological and/or mechanical properties to meet their required functions. Cutting fins may be arranged radially along the longitudinal axis of the base of the stem to improve endosteal contact and resist torsion when implanted. The base of the stem and the flange are plasma-sprayed with titanium (70-100um) and subsequently treated with hydroxyapatite (50-70um) to provide a porous surface to encourage bone and skin integration. The flange is perforated by tiny circumferential holes 0.7mm diameter to mimic the porous structure of deer antler. The peg which is outside the body is coated by plasma-assisted vapor deposition with low surface energy “diamond-like carbon coating, DLC” (2-4 um) which reduces the adhesion of bacteria to the surface of the external part of the implant.

The ITAP device was custom manufactured for each dog or cat using measurements made from CT scans and radiographs. CT and MRI additionally assisted determination of extent of resection required for tumor-free margins (truncation margin). The required dimensions of the implants were achieved to allow insertion of the stem into the distal metaphysis of the radius or tibia or the calcaneus and positioning of the flange in the hypodermal tissue eliminating skin tension. More recently, modification of flange design has allowed attachment of flexor and extensor tendons subjacent to the calcaneus to allow appropriate placing and control of the exoprosthesis in sub-talocural applications.

As no precedent existed for dogs, development of the exoprosthesis has been iterative. 3D modelling of endoprostheses facilitates stress analysis using finite element methodology to determine the strength of the ITAP during anticipated loading conditions (obtained from published biomechanical data for similar breeds). The ITAP 3D model is superimposed on a scaled radiograph of the contralateral limb and measurements obtained of length, angle and
shape of the proposed exoprostheses. An iterative process of design and analysis is undertaken to establish optimal combination of material, cross section and alignment to appropriate the strength of the ITAP under the applied load and producing adequate stiffness in terms of shock absorption and energy return in order to stress-protect the ITAP by exteriorizing the maximum strain focus into the proximal extent of the exoprosthesis. The material chosen for the calcaneal exoprostheses is selective-laser-sintered nylon and for radius and tibia, a Delrin™ shaft to the base of which is attached a semi-constrained multi-directional foot component with Kevlar on rubber impregnated with air-bubbles and shock-absorbing foam-beads. Exoprosthesis design parameters are calibrated to withstand anticipated loads whilst providing a break-point such that in the event of overloading the exoprosthesis will fail first and therefore protect the underlying endoprosthesis. The ground reaction force is considered (1) to allow “rocker motion” during the stance phase in sagittal and frontal planes; (2) to advance cranially as the stance phase progresses to ensure symmetrical gait; (3) to allow “sole” design which provides interface ground-surface friction mimicking shear components of physiological ground reaction force; and (4) to allow “sole” design which is sufficiently compliant to provide shock absorption during impact loading.

A customized external fixation apparatus is constructed to protect the stump-ITAP construct and to facilitate appropriate healing and maturity of the osseous-implant and skin-implant interface, by providing a frame that the patient can walk on for 5-6 weeks. More recent iterations of technique and post-operative rehabilitation are designed to potentially obviate the requirement for frame application in selected patients. Generally, following fitting of appropriate exoprostheses, patients can walk and run and perform all activities which had been possible before pathology was evident, including playing with toys. Subjective gait assessment has been deemed to be equivalent to that which would be expected following a conventional pancarpal or pantarsal arthrodesis in the case of distal radius/tibia implants and restoration of excellent function for calcaneal ITAP patients. Pain-free function with resilient implant-skin interface has been consistently observed, although a minority of patients which had preoperative trauma-associated infection issues, have proved problematic in terms of infection control.

Post-operative radiographic and CT examination has demonstrated good osteointegration with bone abutting the implant. No radiolucency has been appreciated around the HA coated ITAP stem. Thickening of both endosteal and periosteal bone surfaces around the point of load transfer from implant to bone is consistent with bone remodeling. In the case of tendon-dermal ingrowth flange constructs, early experience has been favorable in terms of functional limb use.

The retrieved implant and associated limb from one dog, euthanized because of tumour metastasis, was assessed with owner permission. The histological sections demonstrated incorporation of the flange in dermal tissue with the epidermis abutting onto the stem of the implant. The flange embedded in the dermal tissue was not encapsulated but rather fibroblasts were evident attaching to the hydroxyapatite surface. Histological examination was consistent with satisfactory and resilient ITAP-dermal interface.

The development of and clinical application of ITAP requires significant financial and personal commitment from owners. Financial implications will undoubtedly have a major impact on the potential application and development of ITAP in small animals. However, as awareness of prosthesis use generally increases, such as for total joint replacement of the hip, elbow or stifle, and as recent human and veterinary experience reports lower failure and infection rates with newer endoprostheses for limb salvage, there is likely to be an increase in numbers of animal owners seeking prosthetic technology if future development and clinical application continues to be favorable and results of objective studies demonstrate superior results of such technology. As veterinary professionals, we have a responsibility to offer the
gold-standard of care to our patients. It is for the owners to decide if they wish to avail of such technological advancements or not. The author is of the opinion that it is our responsibility to strive for better treatments for our patients where existing options are suboptimal, but we must do so in a morally and ethically robust fashion and using best-evidence at all times.

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