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The evolution of three-dimensional technology in musculoskeletal oncology

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Musculoskeletal tumours pose considerable challenges for the orthopaedic surgeon during pre-operative planning, resection and reconstruction. Improvements in imaging technology have improved the diagnostic process of these tumours. Despite this, studies have highlighted the difficulties in achieving consistent resection free margins especially in tumours of the pelvis and spine when using conventional methods. Three-dimensional technology – three-dimensional printing and navigation technology – while relatively new, may have the potential to prove useful in the musculoskeletal tumour surgeon's arsenal. Three-dimensional printing (3DP) allows the production of objects by adding material layer by layer rather than subtraction from raw materials as performed conventionally. High resolution imaging, computer tomography (CT) and magnetic resonance imaging (MRI), are used to print highly complex and accurate items. Powder-based printing, vat polymerization-based printing and droplet-based printing are the common 3DP technologies applied. 3DP has been utilized pre-operatively in surgical planning and intra-operatively for patient specific instruments and custom made prosthesis. Pre-operative 3DP models transfer information to the surgeon in a concise yet exhaustive manner. Patient specific instruments are customized 3DP instruments utilized with the intention to easily replicate surgical plans. Complex musculoskeletal tumours pose reconstructive challenges and standard implants are often unable to reconstruct defects satisfactorily. The ability to use custom materials and tailor the pore size, elastic modulus and porosity of the 3DP prosthesis to be comparable to the patient's bone allows for a potential patient-specific prosthesis with unique incorporation and longevity properties. Similarly, navigation technology utilizes CT or MRI images to provides surgeons with real time intraoperative three-dimensional calibration of instruments. It has been shown to potentially allow surgeons to perform more accurate resections. These technological advancements have the potential to greatly impact the management of musculoskeletal tumours. 3D planning models, patient-specific instruments and customized 3DP implants and navigation should not be thought of as separate, but rather, patient-specific adaptation of relevant modes of application should be selected on a case-by-case basis when taking all unique factors of each case into consideration.

1. Introduction

Musculosketal oncology is a subspecialty of orthopaedic surgery that focuses on the diagnosis and multidisciplinary management of patients with benign and malignant tumours of bone and connective soft tissues.

Improvements in imaging technology have improved the diagnostic process of musculoskeletal tumours. Digital X-rays now allow for manipulation of the image contrast, enlargement, brightness, rotation and accurate digital measurement. Nuclear medicine modalities allow for safe, highly sensitive and specific staging. Computer tomography (CT) and Magnetic resonance imaging (MRI) provide three dimensional (3D) detailed anatomic images of the body to guide surgical planning.

Surgical treatment of musculoskeletal tumours comprises a trade-off between adequate resection margins and residual function. Clear operative oncological margins are the primary factor of consideration in tumour resection. In 2008, Cartiaux et al. demonstrated that four experienced surgeons were unable to accurately and consistently obtain adequate resection margins for

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pelvic tumours despite ideal conditions.[1]

The incorporation of 3D printing (3DP) and navigation technology may be useful in the management of musculoskeletal tumours.[2] This review focuses on 3DP and navigation technology, and their applications as a useful adjunct in the pre-operative planning and surgical management of musculoskeletal tumours.

2. Three dimensional printing and musculoskeletal oncology

2.1. Three dimensional printing

Three-dimensional printing is an additive layer manufacturing (ALM) technique. It was first introduced in the 1980s and is now one of the most efficient methods of customizing products from a variety of materials. ALM allows the production of objects by adding material layer by layer rather than subtraction from raw materials as performed conventionally. This enables the production of detailed patient-specific and custom-designed constructs which have not been produced using conventional subtractive methods such as melt/solvent casting, electrospinning, compression/injection molding and porogen leaching.[3]

Improvements in CT and MRI technology now allow for detailed imaging to be done with 1 mm (mm) cuts. 3D printers use the information from a computer aided design (CAD) file derived from CT/MRI imaging to produce specific items. There are a plethora of 3DP techniques available for use in engineering. The three common and relevant types of 3DP in musculoskeletal oncology include powder-based printing, vat polymerization-based printing and droplet-based printing.

A basic understanding of each technique could aid the understanding of its subsequent application to management of musculoskeletal tumours.

2.2. Powder-based printing

Powder-based printing comprises of direct metal laser sintering (DMLS), selective laser melting (SLM), selective laser sintering (SLS) and electron beam melting (EBM). All technologies rely on local heat to fuse powdered materials while differing in powder materials and energy source.[4] Sinistering leads to the formation of porous structures with rough surfaces as the powders are not melted completely. DMLS, SLM and SLS utilize mirrors directing laser beams while EBM utilizes an electron beam directed by electromagnets in a vacuum (resulting in higher cost). SLS is able to utilize a wide range of materials while DMLS exclusively utilizes metal alloys. EBM and SLM use metal alloys and ceramics.

2.3. Vat polymerization-based printing

Vat polymerization-based printing, also known as stereolithography (SLG), continuous direct light processing (CDLP) and direct or digital light processing (DMP), uses an ultraviolet light that cures a vat of liquid photocurable polymer resin one layer at a time. A platform raises the vat as each layer hardens when it comes in contact with the ultraviolet light and is cured. It was the first ALM technique, invented in 1986, used as a surgical model in the planning of craniofacial surgery.[5] The 3DP constructs are exposed to light post curing to enhance the mechanical properties and stability.

2.4. Droplet-based printing

Droplet-based printing jets precise liquid droplet streams onto a substrate layer by layer.[6] Droplet-based printing includes laser-induced forward transfer (LIFT), multijet modeling (MJM), binder jetting (BJ) and wax deposition modeling (WDM). LIFT utilizes a laser focused on a laser-absorbing layer (such as titanium) and heats the metal to gas plasma state to form a vapour pocket. A droplet of ink material is then ejected into the pocket receiving the substrate. MJM is an inkjet printing process that deposits casting wax materials or photocurable plastic resin layer by layer. WDM uses molten wax which solidifies when cooled. BJ which can be also considered as a powder-based technology, jets a liquid binding agent (adhesive) to bind powder particles (metals, polymers, ceramics).

3. Three dimensional printing in musculoskeletal oncology

Over the past two decades, ALM has become increasingly popular due to the ability to control the overall structural architecture (porosity and pore distribution), size and shape, material composition and material chemistry (mechanics and degradation) of the custom, high-throughput and highly-reproducible constructs. More than 10,000 customized DMLS truss implants have been implanted in patients undergoing spinal surgery between 2013 and 2016.[7] In musculoskeletal oncology, 3DP has been used for pre-operatively in the production of models useful for surgical planning and intra-operatively for patient-specific instruments (PSI) and custom made prosthesis.

3.1. Pre-operative planning models

CT and MRI provide good 3D visualization of bony and soft tissues respectively and, traditionally, surgeons have to mentally integrate this information to formulate a pre-operative plan. Patients with musculoskeletal tumours, especially of the pelvis and spine, often present with altered and unique anatomy. Despite ideal conditions, some surgeons may have difficulty carrying out planned resections.[1]

3D printed models have been useful for transferring information to the surgeon to allow for more detailed surgical planning for complex oncological patients including ENT, head and neck, urology, cardiothoracic and orthopaedic surgery.[8] With patient-specific 3D models, surgeons can analyze this processed information to formulate more detailed pre-operative planning and surgical intervention.

Tam et al. used 3DP powder-based printing to create an accurate model of a patient presenting with a large scapular osteochondroma from CT images.[9] The model produced aided subsequent surgical management of the geometrically complex tumour. Ma and colleagues incorporated 3DP SLG technology to formulate a patient-specific 3D printed model and guiding templates for eight patients undergoing distal femur osteosarcoma resection from a combination of CT and MRI images.[10] It required 10 hours and costed an estimated 30 dollars for both femoral models and guiding templates. The improved pre-operative planning and guiding templates resulted in precise resection of the bone, accurate implantation of allografts, decreased blood loss, reduced surgical time and decreased radiation. Similarly, in excision of primary malignant bone tumour of the cervical spine, preoperative 3D printed models improved anatomical understanding and assisted in surgical planning.[11]

Besides use by surgeons for pre-operative planning, patient-specific 3DP models can be utilized by medical students or trainees for education purposes and therapists or patients for better understanding of the disease. Limitations of the 3DP model include the possibility of processing inaccuracies. However, this is unlikely as most 3DP have minimum resolutions of at least 0.10 mm which is unlikely to have an impact on accuracy as most current CT and MRI machines use 1 mm imaging cuts.

3.2. Patient specific instruments

PSI are 3D printed intra-operative instruments, conceptually introduced in the 1990s by Radermacher et al.,[12] designed from digital or pre-operative 3D models of patient anatomy to replace computer navigation, which will be discussed later. The customized instrument is utilized with the intention to easily replicate surgical plans. PSI have been reported in guiding hip and knee arthroplasty,[13] pedicle screw insertion for cervical and thoracic[14] spine surgery and difficult osteotomies in deformity correction for fracture malunion.[15]

In 2012, Wong et al. first demonstrated the use of PSI in a patient with low grade osteosarcoma of the femur.[16] Following proof of concept of PSI in bone tumour surgery on a cadaver leg, a thermoplastic cutting jig was 3DP based on CT imaging of the patient. The coronal and sagittal images showed the achieved resection to differ by < 1 mm from the planned resection. Bellanova et al.[17] applied SLS 3DP technology to design PSIs to guide tumour resection cuts and allograft shaping cuts for four pediatric patients undergoing tibial bone sarcoma resection and bone-bank allograft reconstruction. All resection margins were tumour-free. Post-operative imaging revealed satisfactory host-graft contact and no evidence of recurrent disease.

A cadaveric study comparing 3DP PSI designed cutting jigs and traditional manual resection found the mean maximum deviation from the preoperative plan to be 9.0 mm for the conventional manual group and 2.0 mm for the custom-jig group ($p < 0.001$). The percentages of times the maximum deviation was greater than 3 mm and greater than 4 mm was 100% and 72% for the conventional manual group and 5.6% and 0.0% for the custom-jig group, respectively.[18] A second cadaveric study yielded similar results.[19] PSI use for a series of 11 patients with pelvic bone tumours[20] achieved tumour free resection margins for all patients with an average error in resection margin of 0.8 mm.

The limitations of PSI include the need for adequate bone exposure intraoperatively to ensure a satisfactory fit. This could be technically challenging during the operation due to surrounding soft tissue and muscle. Also, the lack of real time feedback when using PSIs, as compared to navigation systems, could potentially result in incorrect placement. Inaccurate placement of PSI could result in the subsequent incorrect guided procedure and may result in deviation from the pre-operative plan. This may be potentially reduced with an increase in contour of bone surfaces.[21] PSI also requires substantial preoperative planning and a timeframe of manufacturing of four to five days. This could mean that any growth in the tumour during this period could result in a mismatch of PSI and patient anatomy and an intralesional or inaccurate excision.

3.3. Custom made prosthesis

Several techniques exist for tumour reconstructive surgery in musculoskeletal oncology: allografts, autografts, recycled bone and endoprosthesis. When patient's anatomy falls outside standard implant size ranges and customized implants are required, especially of the pelvis or spine, traditional subtractive manufacturing technology is limited. The use of detailed CT/MRI imaging enables the production of highly customized implants.

Furthermore, modern 3DP techniques allow for porous structure which facilitates osteointigration and the possibility to reduce stiffness mismatch at bone-implant junctions.[22] Biocompatible materials such as 316 L stainless steel, titanium-6aluminium-4vanadium and cobalt-chromium are utilized using SLM or EBM for 3DP custom implants. The ability to tailor the pore size, elastic modulus and porosity of the 3DP prosthesis to be comparable to the patient's bone allows for a potential patient-specific prosthesis with unique incorporation and longevity properties.[23]

With no available modular prosthesis to reconstruct the clavicle, scapula, and ilium, Han et al. utilized 3DP EBM technology to produce patient-specific prostheses.[24] No surgical complications of limb length discrepancy, screw loosening, and implant breakage were observed and the Musculoskeletal Tumor Society (MSTS) scores were 93, 73, and 90% for patients with clavicle Ewing sarcoma, scapular Ewing sarcoma, and pelvic chondrosarcoma respectively.

Wong and colleagues utilized 3DP to design a customized implant and PSIs to reproduce planned resection for a patient with pelvic chondrosarcoma.[23] Resection margins were clear and errors of the achieved resection and implant position were deviating 1–4 mm from the pre-operative plan. No tumor recurrence and implant loosening were noted at 11 months after surgery. 3DP was also used successfully for revision reconstruction of metaphyseal osteosarcoma initially treated with intercalary allograft reconstruction complicated by infection.[25] At a follow up of 26 months, knee joint motion was 0–130° and an Enneking functional evaluation score of 28 out of 30.

Chen et al. combined the use of navigation technology and a 3DP custom implant for the reconstruction surgery of a patient with pelvic sarcoma.[26] They developed a novel navigation system for the 3DP implant and demonstrated an improvement in precision of implantation of three to five times: 0.75 ± 0.18 mm (with navigation) compared to 3.13 ± 1.28 mm (without navigation).

Choy et al. used a 3DP patient-specific prosthesis to reconstruct a pseudo-myogenic-hemangio-endothelioma of the T9 vertebrae.[27] Custom design features included porous titanium end plates, corrective angulation of the implant to restore sagittal balance, and pedicle screw holes in the 3D implant to assist with insertion of the device. Following successful surgery, the patient returned to playing sports at 3 months. Radiologic follow-up at 6 months indicated the implant was well positioned and had integrated with the adjacent end plates. Similarly, Xu et al.[28] reported the use of a custom 3DP vertebral body used for the reconstruction of the upper cervical spine in a young patient with a Ewing's sarcoma. Immediate stability was achieved and there was osteointegration without subsidence or displacement one-year post-operatively. Wei et al. reported the successful use of 3DP for reconstruction surgery of sacrectomy for recurrent sacral chordoma.[29]

Wang et al. reported the largest cohort of eleven patients till date who underwent wide resection of peri-acetabular malignant bone tumours and reconstruction arthroplasty using personalized 3DP hemipelvic prostheses. The mean MSTS-93 lower extremity functional outcome score was 19.2 (range, 13–25) and there was no evidence of aseptic loosening, bone resorption or peri-prosthetic fractures during the mean follow-up of 15.5 months.

Compared with traditional manufacturing methods, 3DP may provide some benefits. 3DP technology can produce metal surfaces with porous scaffolds. These allow host bone to grow inside the construct to facilitate integration. Potential shorter operating times may decrease intra-operative blood loss.[30] 3DP may be also be used to produce PSI which can be used concurrently to replicate the planned resection planes to achieve satisfactory implant positioning.

While improvements in technology have allowed 3DP prosthesis to be used successfully for reconstruction of complex bone tumour defects, high quality evidence is lacking. While randomized control trials may be unfeasible, larger cohort studies or multi-institutional studies are needed to adequately compare the use of 3DP with other reconstructive options. Concerns of high implant costs, time lags in the designing and manufacturing of implants to meet surgical deadlines, lack of intraoperative flexibility of the implant and difficulty in achieving accurate implant placement[31] may slow progress.

4. Navigation technology and musculoskeletal oncology

4.1. Navigation technology

The use of navigation technology in neurosurgery to determine tumour location preoperatively and guide surgical resection produced improved margins and outcomes in subsequent resections.[32] Navigation guided pedicle screw insertion in spine surgery demonstrated reduced inaccuracies in screw placement and reduced radiation exposure.[33] Consequent adaptations of navigation technology in ENT,[34] urology,[35] orthopaedic trauma[36] and joint arthroplasty[37] similarly show improved resection margins, more accurate implant placement and improved surgical outcomes.

4.2. Navigation technology and musculoskeletal oncology

Navigation based technology in musculoskeletal oncology is an imaged-based system. This is in contrast to imageless systems which rely solely on the information obtained from registration of patient's anatomy intra-operatively following adequate surgical exposure. A hand-held mapping tool is used intraoperatively by the surgeon on various bony landmarks to provide the imageless-navigation system with sufficient data and a surgical plan is formulated intraoperatively.

Similar to 3DP, navigation technology requires pre-operative imaging (CT, MRI, PET-CT) to assess tumour size, soft tissue involvement, extent of intraosseous disease and anatomical relation to important neurovascular structures. CT is superior at imaging bone while MRI is superior at imaging soft tissues. PET-CT may provide additional value in distinguishing tumour tissue from scar tissue secondary to previous radiation/resection in cases of tumour recurrence. A technique described by Wong et al.[38] describes the fusion of these imaging modalities to form a more accurate 3D representation of patient anatomy. This information is interpreted by a computer program and consequently utilized by the surgeon to develop a pre-operative plan.

Navigation technology in musculoskeletal oncology requires crucial extensive intraoperative registration of patient anatomy with information from the pre-operative imaging analyzed by the software. Intraoperative registration is operator dependent and the main determinant of navigation success. Bony landmarks (e.g. iliac crest tubercle, anterior superior iliac spine, spinous processes) have a fixed position and are hence used for registration as opposed to soft tissue landmarks. An infra-red camera captures information of the patient anatomy from a navigation probe used by the surgeon to complete the registration and calibration process. Once complete, an image of the fused CT/MRI/PET-CT is displayed with the real-time position of the navigation probe on the screen. If necessary, surgical instruments can be calibrated to display their 3D position as well. This potentially allows for more precise resection with real-time feedback.

Cartiaux et al. demonstrated that surgeons were unable to accurately and consistently obtain adequate resection margins for pelvic tumours despite ideal conditions. The probability of a surgeon obtaining a 10-mm surgical margin with a 5-mm tolerance above or below, was 52% and the resulting degree of contact at the host-graft junction was poor.[1] The group demonstrated significantly improved resection accuracy in a subsequent study using navigation[39] – 2.8 mm inaccuracy for the navigated procedure as compared to 11.2 mm for the conventional cutting procedure.

Jeys and colleagues demonstrated a reduction in intralesional resection rates from 29% to 8.7% with the use of intraoperative navigation in 31 patients with musculoskeletal tumours of the pelvis and sacrum.[40] The registration error was <1 mm in all cases and no complications related to navigation use. The use of navigation allowed the preservation of sacral nerve roots ($n = 13$), resection of otherwise inoperable disease ($n = 4$) and the avoidance of hindquarter amputation ($n = 3$). When comparing the outcomes of navigation-guided resections with pre-operative planned resection, Aponte-Tinao et al. found a mean difference of 2.43 mm.[41]

Cho et al. demonstrated clear resection margins in all 18 patients with metaphyseal or pelvic tumours.[42] Local recurrence occurred in 2 patients who had tumours resected from the pelvis. Similarly, Young et al. demonstrated clear margins for 18 patients with diaphyseal and pelvic tumours undergoing navigation guided resection surgery.[43]

Li et al. described the use of navigation technology and its utility in complex limb salvage surgery for tumours around the proximal humerus and knee with clear resection margins in all patients.[44–46] Others reported similar results when using navigation surgery in complex joint preserving surgery.[47,48]

A study by Lall and colleagues demonstrated better fit and increased contact between allograft implant and resection planes during reconstructive surgery with the use of navigation technology.[49] This could potentially result in improved bone healing and decreased non-union rates, which are reported to be as high as 27% in bulk allograft reconstruction.

Navigation provides real-time intraoperative feedback and allows for more accurate resection in complex musculoskeletal oncology cases with improved outcomes. However, some limitations prevent widespread adoption of this technology. They include the increased learning curve of utilizing this technology, the cost of the navigation systems, increased pre-operative planning time, potentially increased intra-operative surgical time (due to set up and utilization of the system), need for extra manpower within the operation theatre and registration errors which may potentially guide inaccurate or intralesional resection.[48]

As mentioned above, PSI were introduced to replace navigation technology. When compared to computer-navigation assisted techniques which require navigation equipment and a machine operator, operating time with PSI could be potentially reduced.[50] PSI could be more cost effective as the technology is on a pay-per-use basis and has a minimal learning curve when compared to computer navigation. The use of custom PSI may produce more accurate results than the computer-navigation as computer navigation orientates the surgeon to the starting point of the resection cut, while custom PSI could potentially provide the trajectory for the entire cut.[18] Further studies comparing the use of computer navigation and PSI in musculoskeletal tumour resection are necessary before any conclusion can be made.

Navigation technology and PSI do not have to be mutually exclusive. A potential improvement could be the use of navigation technology to provide intraoperative real-time feedback and confirm accurate placement of PSI prior to resection, similar to the study by Chen et al. where navigation technology was utilized to complement the implantation of 3DP implants.[26]

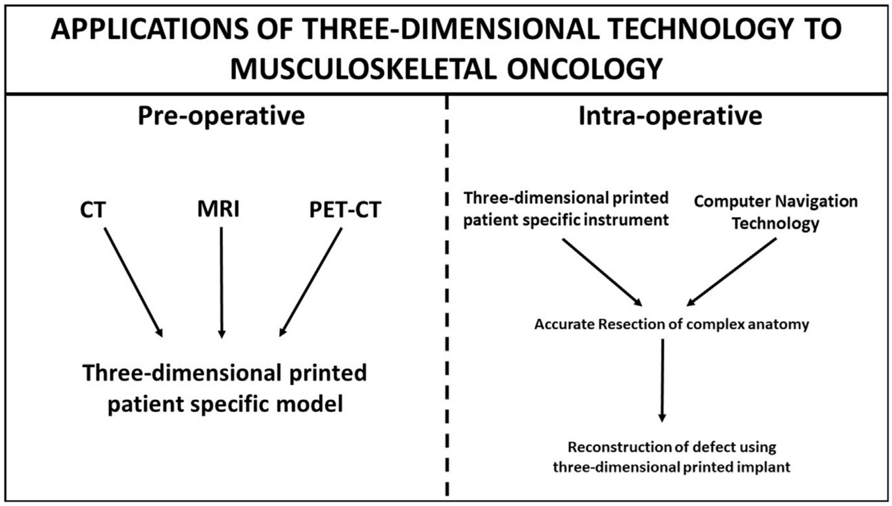

Fig. 1. Three dimensional technology in musculoskeletal oncology.

5. Conclusion

In summary, technological advancements in recent years have allowed navigation and 3DP technology to become useful adjuncts in the management of complex musculoskeletal tumours. musculoskeletal oncology is a complex multidisciplinary specialty with each case being unique due to patient-specific, surgeon-specific and disease-specific factors. The various modes of application – navigation, 3D planning models, PSI and customized 3DP implants – should not be thought of separately. Rather, patient-specific adaptation of relevant modes of application should be selected on a case-by-case basis when taking all unique factors of each case into consideration (Fig. 1).

References

1. Cartiaux O, et al. Surgical inaccuracy of tumor resection and reconstruction within the pelvis: an experimental study. *Acta Orthop*. 2008;79(5):695–702.
2. Morris GV, et al. Navigation in musculoskeletal oncology: an overview. *Indian J Orthop*. 2018;52(1):22–30.
3. Kang HW, et al. A 3D bioprinting system to produce human-scale tissue constructs with structural integrity. *Nat Biotechnol*. 2016;34(3):312–319.
4. Wong KV, Hernandez A. A review of additive manufacturing. *ISRN Mech. Eng.* 2012;2012:1–10.
5. Mankovich NJ, Cheeseman AM, Stoker NG. The display of three-dimensional anatomy with stereolithographic models. *J Digit Imag*. 1990;3(3):200–203.
6. Murr LE, Johnson WL. 3D metal droplet printing development and advanced materials additive manufacturing. *J. Mater. Res. Technol.* 2017;6(1):77–89.
7. Chya-Yan L, Murat G. Current and emerging applications of 3D printing in medicine. *Biofabrication*. 2017;9(2):024102.
8. Matsumoto JS, Morris JM, Rose PS. 3-dimensional printed anatomic models as planning aids in complex oncology surgery. *JAMA Oncol.* 2016;2(9):1121–1122.
9. Tam MD, et al. 3-D printout of a DICOM file to aid surgical planning in a 6 year old patient with a large scapular osteochondroma complicating congenital diaphyseal aclasia. *J Radiol Case Rep*. 2012;6(1):31–37.
10. Ma L, et al. 3D-printed guiding templates for improved osteosarcoma resection. *Sci Rep*. 2016;6:23335.
11. Xiao J-r, et al. En bloc resection of primary malignant bone tumor in the cervical spine based on 3-dimensional printing technology. *Orthop Surg.* 2016;8(2):171–178.
12. Radermacher K, et al. Computer assisted orthopaedic surgery with image based individual templates. *Clin Orthop Relat Res*. 1998;354:28–38.
13. Buller L, et al. The use of patient-specific instrumentation improves the accuracy of acetabular component placement. *J Arthroplasty*. 2013;28(4):631–636.
14. Mac-Thiong J-M, et al. Evaluation of a transpedicular drill guide for pedicle screw placement in the thoracic spine. *Eur Spine J*. 2003;12(5):542–547.
15. Takeyasu Y, et al. Preoperative, computer simulation-based, three-dimensional corrective osteotomy for cubitus varus deformity with use of a custom-designed surgical device. *J Bone Joint Surg*. 2013;95(22):e173.
16. Wong KC, et al. Use of a patient-specific CAD/CAM surgical jig in extremity bone tumor resection and custom prosthetic reconstruction. *Comput Aided Surg*. 2012;17(6):284–293.
17. Bellanova L, Paul L, Docquier P-L. Surgical guides (Patient-Specific instruments) for pediatric tibial bone sarcoma resection and allograft reconstruction. *Sarcoma*. 2013;2013:1–7.
18. Khan FA, et al. Surgical technique: computer-generated custom jigs improve accuracy of wide resection of bone tumors. *Clin Orthop Relat Res*. 2013;471(6):2007–2016.
19. Sallent A, et al. How 3D patient-specific instruments improve accuracy of pelvic bone tumour resection in a cadaveric study. *Bone & Joint Res.* 2017;6(10):577–583.
20. Gouin F, et al. Computer-assisted planning and patient-specific instruments for bone tumor resection within the pelvis: a series of 11 patients. *Sarcoma*. 2014;2014:1–9.
21. Wong KC. 3D-printed patient-specific applications in orthopedics. *Orthop Res Rev*. 2016;Vol. 8:57–66.
22. Ryan G, Pandit A, Apatsidis D. Fabrication methods of porous metals for use in orthopaedic applications. *Biomaterials*. 2006;27(13):2651–2670.
23. Wong KC, et al. One-step reconstruction with a 3D-printed, biomechanically evaluated custom implant after complex pelvic tumor resection. *Comput Aided Surg*. 2015;20(1):14–23.
24. Fan H, et al. Implantation of customized 3-D printed titanium prosthesis in limb salvage surgery: a case series and review of the literature. *World J Surg Oncol*. 2015;13:308.
25. Lu M, et al. Uncemented three-dimensional-printed prosthetic reconstruction for massive bone defects of the proximal tibia. *World J Surg Oncol*. 2018;16:47.
26. Chen X, et al. Image-guided installation of 3D-printed patient-specific implant and its application in pelvic tumor resection and reconstruction surgery. *Comput Meth Progr Biomed*. 2016;125:66–78.
27. Choy WJ, et al. Reconstruction of thoracic spine using a personalized 3d-printed vertebral body in adolescent with T9 primary bone tumor. *World Neurosurg*. 2017;105:1032. e13-1032.e17.
28. Xu N, et al. Reconstruction of the upper cervical spine using a personalized 3d-printed vertebral body in an adolescent with ewing sarcoma. *Spine(Phila Pa 1976)*. 2016;41(1). E50-4.
29. Wei R, et al. One-step reconstruction with a 3D-printed, custom-made prosthesis after total en bloc sacrectomy: a technical note. *Eur Spine J*. 2017;26(7):1902–1909.
30. Wang BC, et al. Computer-aided designed, three dimensional-printed hemipelvic prosthesis for peri-acetabular malignant bone tumour. *Int Orthop*. 2018;42(3):687–694.
31. Unwin PS, Eshraghi A. Custom implants. In: *Computer-assisted Musculoskeletal Surgery*. Springer International Publishing; 2016:181–198.
32. Kurimoto M, et al. Impact of neuronavigation and image-guided extensive resection for adult patients with supratentorial malignant astrocytomas: a single-institution retrospective study. *min - Minimally Invasive Neurosurgery*. 2004;47(5):278–283.
33. Kraus MD, et al. Can computer-assisted surgery reduce the effective dose for spinal fusion and sacroiliac screw insertion? *Clin Orthop Relat Res*. 2010;468(9):2419–2429.
34. Vorbeck F, et al. Experiences in intraoperative computer-aided navigation in ENT sinus surgery with the Aesculap navigation system. *Comput Aided Surg*. 1998;3(6):306–311.
35. Rassweiler J, et al. Surgical navigation in urology. *Curr Opin Urol*. 2014;24(1):81–97.
36. Khoury A, et al. Computer-assisted orthopaedic fracture reduction. *Current Orthopaedic Practice*. 2011;22(1):109–115.
37. Ryan JA, Jamali AA, Bargar WL. Accuracy of computer navigation for acetabular

component placement in THA. *Clin Orthop Relat Res*. 2009;468(1):169–177.
38. Wong KC, et al. Image fusion for computer-assisted bone tumor surgery. Clinical Orthopaedics and Related Research. 2008;466(10):2533–2541.
39. Cartiaux O, et al. Computer-assisted planning and navigation improves cutting accuracy during simulated bone tumor surgery of the pelvis. *Comput Aided Surg*. 2013;18(1–2):19–26.
40. Jeys L, et al. Can computer navigation-assisted surgery reduce the risk of an intralesional margin and reduce the rate of local recurrence in patients with a tumour of the pelvis or sacrum? *Bone & Joint J.* 2013;95B(10):1417–1424.
41. Aponte-Tinao LA, et al. Multiplanar osteotomies guided by navigation in chondrosarcoma of the knee. *Orthopedics*. 2013;36(3). p. e325-e330.
42. Cho HS, et al. The outcomes of navigation-assisted bone tumour surgery minimum three-year follow-up. *J Bone Joint Surg*. 2012;94B(10):1414–1420.
43. Young PS, Bell SW, Mahendra A. The evolving role of computer-assisted navigation in musculoskeletal oncology. *Bone & Joint Journal*. 2015;97B(2):258–264.
44. Li J, et al. Precise resection and biological reconstruction under navigation guidance for young patients with juxta-articular bone sarcoma in lower extremity. *J Pediatr Orthop*. 2014;34(1):101–108.
45. Li J, Shi L, Chen G-j. Image navigation assisted joint-saving surgery for treatment of bone sarcoma around knee in skeletally immature patients. *Surg. Oncol.* 2014;23(3):132–139.
46. Li J, et al. Irregular osteotomy in limb salvage for juxta-articular osteosarcoma under computer-assisted navigation. *J Surg Oncol*. 2012;106(4):411–416.
47. Fan H, et al. Surgical technique: unicondylar osteoallograft prosthesis composite in tumor limb salvage surgery. *Clin Orthop Relat Res*. 2012;470(12):3577–3586.
48. Cho HS, et al. Joint-preserving limb salvage surgery under navigation guidance. *J Surg Oncol*. 2009;100(3):227–232.
49. Lall A, et al. Comparison of surface area across the allograft-host junction site using conventional and navigated osteotomy technique. *Sarcoma*. 2012;2012:197540.
50. Wong K-C, et al. Patient-specific instrument can achieve same accuracy with less resection time than navigation assistance in periacetabular pelvic tumor surgery: a cadaveric study. *Int. J. Comput. Assist. Radiol. Surg.* 2015;11(2):307–316.