Computer assisted surgery in orthopaedic oncology
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General discussion and future perspectives
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The aim of this thesis was to investigate the value of the use of CAS in orthopaedic oncology, either directly measured in accuracy or in clinical results. The question is also proposed as to whether CAS-based objective orientation could result in improved or new surgical procedures. As the use of CAS has consisted of a wide range of diagnoses and procedures, the first part of the discussion deals with direct clinical use, indications and reports in the literature, and will be broken down into the four basic techniques as described in Chapter Two. The core of the discussion will deal with the technique, offering observations on current system accuracy, system use, evaluation of the current tools and the trend of CAS use in orthopaedic surgery and orthopaedic oncology. The last part of the discussion will analyse current CAS use, describe current issues with CAS workflow, list its benefits and provide future perspectives.

Clinical use

Intralesional treatment

The largest number of clinical procedures reported in this thesis dealt with the intralesional treatment of benign, low-grade and intermediate-grade bone tumours. As Chapter Four has discussed specifically for atypical chondroid tumours (ACT)/chondrosarcoma grade 1 (CHS1) and Chapter Two generally for multiple diagnoses, CAS is a technologically superior alternative to standard fluoroscopy. Intralesional treatment, sometimes supported with adjuvants, is also the standard treatment for some of the most common orthopaedic oncology lesions. Surprisingly, the scientific literature reports little about CAS use in intralesional treatments.

Lee et al. described in 2012 that computer-guided curettage is beneficial for the treatment of ‘deeply seated or multi-cystic’ lesions or benign bone tumours close to the cartilage (1). They used image fusion as a tool to observe the effect of the procedures and declared the technique safe if the ‘thickness of subchondral bone’ was greater than 3 mm. The authors also described the lack of a method to delineate progression, possibly resulting in over-curettage. Wong et al. described the use of CAS to assist in the endoscopic removal of six benign bone tumours, offering a minimally invasive approach (NEAT) (2). Somewhat related are the multiple descriptions of the use of CAS, in combination with high-speed burrs, to treat osteoid osteomas in the spine and the long bones (3). An Italian group even described the successful use of a combination of CAS and video-assisted surgery.
(VATS) for the treatment of an osteoid osteoma in the spine (4). All these publications were case reports or small series.

While the new World Health Organisation (WHO) classification has downgraded the low-grade malignant diagnosis CHS-1 to the intermediate ACT, underpinning the need for more watchful waiting, treatment for active or larger lesions is still required. As Lee et al. have stated, there is also benefit in applying CAS to other lesions, either for locally aggressive lesions (giant cell tumours) or in anatomically difficult locations as the femoral neck and head. Moreover, it can be a radiation-free, technologically superior alternative to 2D fluoroscopy for standard curettage procedures.

Chapter Five is the only comparative study in the literature using CAS for the curettage of bone tumours. The study is also one of the larger published series on the treatment of ACT/CHS-1. It underlines not only the need for accuracy in the procedure but also in the measurement and definition of the postoperative result. Even before specific procedure-focused applications, CAS curettage was at least clinically equivalent to fluoroscopy use in ACT treatment without relying on ionising radiation. CAS curettage takes equally as long and may potentially be even faster than fluoroscopy-based curettage. Arguably CAS curettage, as discussed in Chapter Two, is better in difficult anatomical positions, for example fibrous dysplasia of the femoral head or pelvis.

Other benefits are likely to be identified in the future for accurate intralesional treatment resulting in an exactly known size of the defect. Finite-element analysis, for example, can be used to select the best place to create a bone window, optimal reconstruction material, and positioning and type of prophylactic plating (5). As described in this study, the use of CAS could decrease the associated fracture risk. Neither the software nor the hardware are yet specialised for the task of highly accurate curettage though. As the surgeon receives no feedback on progression, there still is a potential for over-curettage with an increased risk of fracture, or under-curettage and thus recurrence.

The need to attach trackers to standard curettes introduces a source of inaccuracy as the attachment may become instable, reducing the potential benefit of the CAS system. Furthermore, as current systems display instruments as 2D lines, the actual spatial orientation of the tool is not visible. This also makes it difficult to work with asymmetrical tools that can enable full curettage through smaller bone windows. With smart tools, aware of their own orientation, percutaneous treatment such as a NEAT-type procedure without the endoscope and with progress tracking becomes an attractive possibility.

An alternative for CT-based CAS procedures as presented in Chapters Two and Four is virtual fluoroscopy (C-arm-based computer-assisted surgery) (6). This is a
hybrid technology that uses CAS and an isometric c-arm-type scanner to track the lesions and the instruments, with automated image acquisition and matching. CT-based CAS systems are often capable of doing both modes, also allowing image fusion (CT/MRI, etc.) on the acquired image. The main advantage is the ability to check the progress of the procedure. The image quality of this type of imaging systems however is not as high as that of standalone CT-scanners (7). Furthermore, as preoperative scans are often already required during the diagnostic process, the radiation dose to the patient is higher. These two techniques on spatial accuracy for curettages have not yet been compared.

Another new alternative technology for the percutaneous treatment of small lesions is radiofrequency ablation (RFA). This technique depends on accurate positioning of the RFA needles and heating of the tissue around the tip of the needle. CT guidance is often used for the placement, yet the technique can be combined with a navigation system to improve positioning accuracy (8). This increase in positioning accuracy together with models of heat-flow could lead to accurate multi-point treatment of larger lesions.

There are not enough data available for a definitive conclusion on CAS as an alternative to fluoroscopy. The use of CAS however is ionising radiation-free, accurate in three dimensions and oncologically safe, and has promising future applications, possibly in conjunction with other innovative techniques. Better scientific reporting is needed to discern between residue and recurrence cases, and to enable comparison of surgical techniques.

**Image-based resections**

Chapters Two and Three discuss the application of image-based CAS on osteotomies.

**Pelvis & sacrum**

Pelvic and sacral osteotomies are by far the most studied procedures within the CAS field. This is with reason, as the treatment of deep-seated, often high-grade lesions in an anatomically complex region is regarded as extremely demanding. There is ongoing development in chemotherapy for Ewing sarcoma, high-grade chondrosarcoma and osteosarcoma, yet radical surgical treatment of a solitary sarcoma remains critical (9-11). Reports in the literature show a relatively high rate of inadequate (intraleisonal or smaller than required) margins (12-14). Inadequate pelvic and sacral margins in high-grade sarcoma were associated with significantly worse clinical outcome and local recurrence (15, 16). Primary pelvic bone tumours overall were even associated with significantly worse clinical results than those in the limbs (17). Experimental research has shown the potential inaccuracy of freehand resection in the pelvis (18). As overviews of CAS use have argued, there is a possible
benefit to the additional accuracy of CAS use (19,20).

The first navigated pelvic and sacral resections were described in 2004 by Hüfner et al. for two cases and by Krettek et al. for one periacetabular sarcoma (21,22). All three were successful. Reijnders et al. reported the radical resection of two high-grade sarcomas (23). So et al. described surgical workflow with CAS and reported two successful pelvic procedures with an average deviation of planes of 6 mm over three planes, as part of a larger case series (24). Wong et al. described the use of CT/MRI fusion to improve planning and identification of margins (25). The same group has published papers on the successful use of integration of computer-aided design (CAD) planning and custom prosthesis use for reconstruction (20, 26). Docquier et al. reported using CAS for both a successful resection and allograft reconstruction (27).

In recent years larger case series with longer-term follow-up have been published. Cho et al. published about seven pelvic and sacral resections, part of a larger study of 18 patients. Clear margins were achieved in all resections; there were two local recurrences in the pelvis at a minimum follow-up of three years (25). Wong et al. achieved wide resection margins in 16 cases and marginal resections in five, in a study that included 12 pelvic and sacral resections on a total of 21 cases. Local recurrences were found at a mean follow-up of 39 months in four cases that had had marginal resection; three of these were in the sacral region (20). Young et al. described eight CAS-assisted pelvic sarcoma resections, all with clear margins, and eight planned planes within 5 mm of the planning and one with a 5-mm deviation due to surgeon planning errors. All patients were alive and recurrence-free at a mean follow-up of 25 months (28). Jeys et al. has published the largest case series on pelvic resections, a study of 31 patients (17). A clear resection margin was achieved in the bone in all cases; overall intralesional resection rate was 8.7%. At a follow-up of 13.1 months, four patients had a local recurrence. Chapter Two presents similar results. Out of 17 pelvic resections, 15 had clear margins (R0 resection) with one intralesional R2 resection in bone and one R1 soft-tissue margin. There were three recurrences.

The indication of CAS for pelvic and sacral resections, while not tested in a direct randomised controlled trial, seems clear. Out of a total of 91 reported procedures in the literature there was only one intralesional resection in bone reported (1%) and five in total (5%) if soft tissue margins were counted, in a wide case mix including lesions of all grades. The only occurrence of an intralesional resection in bone was in our case series. As discussed in that paper, a direct cause was not identified. While there is a possible bias, given that only early adopters with positive CAS experience are likely to publish case reports, these results are very good. Large overview papers on pelvic resections have reported intralesional resection rates, unknown if in bone or soft tissue, of at least 26% (Ozaki et al.) and 29% (Jeys et al.) (15, 29). Fuchs et al. reported inadequate margins in 13 of 40 cases, or 33% (30). No papers reporting
cohorts have yet drawn conclusions on oncological parameters because of the length of follow-up. Wong et al. made a first careful conclusion in a review that results at early intervals may be better than comparative studies (20). It is however likely, considering the higher number of radical resections and the risk of recurrence in non-radical resections, that future reports will show clinical improvements.

**Long bones**

Another well-studied CAS application is in multiplanar, often joint-salvage procedures around the joints of the long bones. Great precision and accuracy is required as there tends to be little room for error in the tight planning. The great advantages of joint salvage, with either reconstruction with custom tumour prostheses or grafts, are better proprioception and joint function (31). The multiplanar resection technique – saving part of the longitudinal continuity of the bone – is seen as a safe alternative to segmental resection and modular prosthetic reconstruction, but is also difficult to perform, as argued in Chapters Two, Five and Six.

Cho et al. describe seven patients eligible for joint-salvage surgery (criteria at least 1 cm of epiphysis outside the margin) with lesions in the metaphysis. These were all reconstructed with an allograft and were disease-free at a minimum of three years follow-up (25). According to the authors, the use of MRI datasets was vital to delineate the tumour and achieve accurate results. Kim et al. very thoroughly describe one successful case using MRI guidance, resorbable pin-based matching, a novel matching instrument and an osteoarticular graft (32).

Wong et al. describe eight joint-salvage resections in the long bones. All resections had free margins and deviation was less than 2 mm between planned and achieved planes as measured on the CAS system (31). Most defects were reconstructed using custom-made prostheses in their series. The 3D models were then imported back into the CAS system as DICOM files and used to plan the screw fixation. Aponte-Tinao et al. used CAS for five patients with chondrosarcoma around the knee (33). All margins were clear and accuracy between planned and achieved planes was 2.43 mm. Young et al. describe eight successful resections in the long bones with clear margins (28). So et al. report 11 successful procedures, most with prosthetic reconstructions. Planned versus achieved deviation was 6.8 mm in point-based/surface matching mode (some difficulties) and 2 mm in CT-fluoro matching mode (24).

Li et al. reported in 2014 on joint-salvage procedures in nine paediatric patients with juxta-articular bone sarcomas, mainly in the femur (34). They describe that CAS with CT/MRI image fusion resulted in ‘… an ideal margin as well as preserving the entire or part of the articular surface’, furthermore ‘intra-articular and periarticular structures … were spared’. The conclusion calls for ‘computer-assisted allograft trimming techniques’ for precise shaping of the allograft. Finally, Aponte-Tinao et
al. subsequently reported a massive case series on 66 procedures (likely including the first five cases) (35). All 66 cases had clear margins.

Again, there are a high number of radical resections reported, 98 out of 98 cases in the literature. Chapter Two reports 26 resections, mainly of low-grade or benign lesions, and five high-grade lesions for resection and reconstruction. There was one R1 resection, in a chondrosarcoma grade 1B, out of these 31 procedures. We described the only non-radical resection reported in the literature, with no direct cause found. Overall, the surgical results for these difficult resections are impressive, highlighting the accuracy that CAS adds to this type of demanding surgery.

**CAS osteotomies for non-high grade lesions**

Chapter Two reported on the use of CAS for the resection of non-malignant tumours such as osteochondroma. There are no reports of this in literature. It is possible to argue that the potential benefits do not outweigh the pre-planning and set-up time costs. However, as argued in Chapter Two, these cases provide excellent possibilities to improve understanding and experience with the system as well as gain experience in workflow. Identification of the planes was quick and easy, especially when the osteochondroma was located in an anatomically complex region like the posterior side of the distal femur, the pelvis, or between the tibia and fibula. With enough practice, planning could generally be done between patient switches during anaesthesiological prepping. Set-up time had dropped on average to 6:30 minutes – time that was likely recouped in the procedure as shown for the curettages (Chapter Four).

Given this pelvis and long bone surgical outcome data, the conclusion that there is an absolute added value for CAS in highly complex cases is an obvious one. The experience from our centre, however, is that one should also learn to work with the system, adapt to its workflow, and learn to trust the feedback. If one only reserves CAS for these highly complex cases, full benefits from the added value will not be reaped and a CAS setup will take up too much time. Besides, it’s not possible to operate CAS reliably and reproducibly if it is only used on an occasional basis.

**Additional effect of increased accuracy**

As seen in Chapter Three, the application of navigation has more benefits than only a lower intralesional resection rate. Navigation allowed for more a complex, salvaging surgical plan, fitting in with the trend of limb salvage surgery. Jeys et al. described that ‘in several cases navigation allowed more complex surgical resections and reconstructions […] than [...] possible using traditional methods’ (17). This has resulted in the sparing of critical structures such as nerve roots and the avoidance of amputations, the ability to operate otherwise inoperable tumours, and more functional reconstructions. Other authors described similar views (20, 32, 35).
This thesis offers additional support for that conclusion, as CAS can be used for complex salvaging procedures that are otherwise impossible, adding to the list of critical structures that otherwise could not be spared. Pathologic analysis showed excellent results with a very high number of non-intralesional resections. More follow-up is needed to assess long-term oncological follow-up, but the initial results are promising.

**Image-based resections and reconstructions**

Grafts are an option for reconstruction after joint salvage procedures, pelvic resections or other large bone defects. The benefits and indications of the hemicortical technique were discussed in Chapters Five and Six. Overall graft performance, techniques and indications have been reviewed by Aponte-Tinao et al., underlining both the complexity and the sparing potential of its use (36). As there is some overlap with the multiplanar resections and reconstructions examined in the image-based long-bone resections, this discussion will focus on the use of CAS for the reconstruction of defects using bone grafts.

Docquier et al. reported in 2010 the first use of CAS for the reconstruction of a large pelvic sarcoma (27). The paper described a practice session on a printed model of the pelvis and the subsequent surgery. Target plane coordinates were transferred by means of graft-to-patient registration. As the practice demonstrated a gap due to saw loss, the planning for the graft was moved back to compensate for this. The resection is performed with a guided oscillating saw.

Aponte-Tinao et al. and Chapter Five of this thesis report on an independently developed similar, easy-to-follow technique for exact allograft creation in the long bones (37). The resection planes were copied onto the bone and resected using freehand tools. There was correction for saw loss, to create an exact fit of the donor bone. Aponte-Tinao et al. used imported 3D models of the resection planes during surgery, compared to our technique of planning the planes directly. In a subsequent paper the same group reported a non-union rate of 6% and a complication rate (that includes four non-unions) of 14% in 66 cases (36). The authors state that the non-union rates in their series is lower than in the literature (>10%) but that the complication rate did not differ. Fracture rates specifically were not discussed though. Results in both papers are promising; both mentioned that the technique reduced complexity of multiplanar resection, reconstruction of defects, and increased accuracy and precision.

Young et al. (2015) used CAS as support for the reconstruction of intercalary defects with grafts. They did not direct shape the allograft, but used the navigation to ‘... aid construction with regard to limb length, rotation and overall alignment ...’, by planning an additional axial plane (and likely markings on the bone, to find this
plane during reconstruction) (28). This was a technique similar to what we used for intercalary graft orientation after the computer-assisted allograft shaping, as demonstrated in Chapter Two. This technique is very useful, as bone continuity is lost during resection and reconstructing exact joint/leg orientation with the naked eye is difficult.

An experiment on sawbones by Lall et al. looked at the surface area across the allograft-host junction site. Computer navigation showed a contact area of 43.7% of the optimal surface over 30.5% contact area in freehand resection, measured using pressure paper (38). The authors speculated that the low contact area may be a cause for the significant non-union rate in the literature, and that ‘an increase in contact area using [CAS] may improve rates of bone healing’.

A further increase of accuracy and precision in resection and allograft creation was examined in Chapter Six. It was shown that, in the context of this small study, the already-accurate results of CAS resection and reconstruction could be improved upon. Docquier et al. explored possible sawblock usage to increase accuracy, and dismissed this option based on one paper that described faster and more accurate navigated freehand cuts in arthroplasty compared to saw guides (27). In our experiment, CAS and CAS-guided procedures took somewhat longer, yet the results were good, with CAS comparable to the literature and the CAS-guide slightly better. Accuracy (deviation), precision (positioning and smoothness) and gap all improved over freehand resection. The experiment proved that CAS use can improve accuracy and precision in orientation (finding the planned resection), but that the CAS guide actually helps to execute the planned bone cuts more accurately and precisely.

Another important step to achieve an optimal reconstructive result with a maximum of bone contact is the selection of allografts on three-dimensional shape. In the Netherlands and in many other countries, this is done by matching patient and donor sex, basic measurements and/or 2D radiographs. Paul et al. demonstrated that for pelvic allografts this process was prone to inaccuracies and suffers from interobserver variability (39). Several studies have published more accurate methods for volumetric allograft selection (40, 41). These methods are currently applied in practice in some clinics and bone banks.

Both in experimental and clinical studies, results with the use of navigation for allograft shaping have been excellent. The complexity of the procedure was reduced. Non-union rates were lower than comparative studies in the literature. Fracture rates have not been investigated yet. Better tools can potentially further increase graft creation accuracy and decrease complications associated with lack of smoothness and host-allograft gaps.
(Imageless) prosthesis placement

One of the major changes in orthopaedic oncology in recent decades has been the increasing trend of limb salvage surgery, driven by chemotherapy, improved imaging quality and the availability of modular prostheses. Length of reconstruction increases the need for accuracy as small errors in stem position are magnified. Further, bone stock is limited after large resection so placement has to be accurate the first time.

Image-based placement of custom and pelvic prostheses is the most commonly reported form of CAS-supported prosthesis placement in the literature. Wong et al. have described their extensive experience, mainly with the placement of custom tumour prostheses, both in the long bones and in the pelvis. As stated before, they used navigation not only to achieve the exact resection planes the custom prosthesis is made for, but also to achieve the exact fixing screw positions. In a paper on eight patients an average MSTS score of 29.1 (range 28-30) was found and their scores were, according to the authors, higher than the scores achieved in comparable studies (31). An interesting observation in this paper is that for close joint salvage procedures CAS can benefit survival of the remaining bone ‘as the epiphysis and its capsular and ligamentous attachment no longer have to be fully exposed for reference’, resulting in preservation of blood flow. Young et al. used image-based CAS for conic pelvic implant reconstruction to accurately ‘identify the entry point, direction, and depth of reaming for the coned stem’ (28). This is a technique we have applied as well, in the placement of a stemmed cup (LUMiC), and can confirm its usefulness.

There is, as far as we know, only one other reference to imageless (modular) prosthetic placement in the literature. Cheong et al. discussed in 2011 the application of imageless CAS in tumour prosthesis placement in an unknown number of procedures. The authors were able to ‘minimize leg length discrepancies, improve restoration of the joint line, and address rotational concerns of implant alignment’. Post-procedure limb length discrepancies were no greater than 1.5 cm (42). Further data on implant positioning or oncological parameters was not given.

Chapter Two described similar conclusions in an overview of 14 imageless cases. The technique was in our experience very helpful for length, joint line and rotation reconstruction. We also reported that the use of the imageless measurement mode is useful in exactly marking the resection plane for both safe resection and adherence to resection and reconstruction planning.

Our comparative study on the benefits of imageless CAS in tumour prosthesis placement is still in the follow-up phase, as the only way to discern benefit, without a direct RCT with CT measurement or a recall of patients, is implant survival.
In conclusion, there are not enough data available, either in direct measurements or in implant survival and patient satisfaction data, to draw conclusions on (imageless CAS) prosthetic placement. Expert opinions and small-case series have described this type of CAS application as beneficial in the placement of conical and custom prostheses (image-based) and modular tumour prostheses (imageless). More research is needed.

**Technical evaluation**

**CAS accuracy and the need for improved data gathering**

For every surgical action there is an uncertainty in the spatial positioning of the tool or implant. This has impact not only on the result actually achieved but also on the planning, as this uncertainty has to be factored in. A support system that is precise but not accurate only improves adequate resection rates (tumour plus minimally required margin) if a sufficiently large margin is chosen. While favourable oncological results are the primary goal of tumour surgery, large margins can compromise postoperative functional outcome. The benefits that CAS can provide are thus linked not only to the accuracy of the tool placement but also to the precision with which the supported action is performed.

Current CAS research is mainly focused on the clinical effects of application of CAS to surgical procedures in a specific anatomical area. The structure of this thesis is an example of that. Authors often describe the margins and report on what could be saved that otherwise had to be resected. Yet to better understand the actual accuracy and precision of the CAS systems and its toolset we need clinical measurements. The system error (sometimes reported as matching error), while often reported, is not a real representation of actual system accuracy (43). A further factor that underlines this need is that there is no single, unified CAS workflow. System, software, image quality, registration techniques and tool use differ between clinics. Studies have already found large accuracy differences between surgical systems in imageless (arthroplasty) and image-based (mandibular resections) workflow (44, 45). Ritacco et al. and Abrahams et al. have argued the need for clinical measurement by measuring planned planes versus achieved cutting planes on postoperative imaging (46,47). Cartiaux et al. have evaluated the use of ISO standards for the measurement of osteotomy accuracy for this exact purpose (48).

Improved data gathering through image fusion can furthermore benefit the entire field of orthopaedic oncology. Our current standard of reporting for margins is either based on the Enneking criteria (wide, marginal, intralesional) or the R classification (R0 radical, R1 microscopic involvement, R2 macroscopic involvement) (49, 50). The
minimal margin over the whole resection is decisive for the classification. Wong et al. argue that ‘a judgement of clear surgical margins is based on sampling ... and may underestimate the actual incidence of involved margins’ (20). What’s more, resections with the same classification can have large differences in average margin. Another argument is that including postoperative margin measurements in our workflow is likely to not only benefit scientific research but also support pathological examination (51). This enables fast identification of tumour spill sites or areas at risk due to small margins. It would therefore be good to have the resected specimen CT-scanned before histological examination. In postop examination of procedures where normal pathological examination for margins is not possible, like curettages, it is already standard care to perform a baseline MRI as a postoperative check.

Measurement data achieved with different modalities and surgical toolsets, resulting in values for precision and accuracy, can likely be used to enhance our surgical planning and support radical decisions in difficult edge cases. Combining this uniform data with clinical follow-up can drive the discussion on required margins. Finally, as we are very likely past the stage of an ethically acceptable randomised controlled trial on CAS for high-grade sarcoma, this data can be critical in the scientific evaluation of surgical techniques.

**CAS system use**

There are different strategies to CAS use, both for matching and instrumentation, in the literature. Most reports and procedures in this thesis used point-based matching and surface matching. Some different strategies described were direct matching on MRI images using resorbable pins as fiducial markers by Cho et al. and Kim et al. (32,52). Cho et al. also used K-wires for CT-based matching. These techniques may reduce the chances of large mismatches. The downsides are that a small procedure is needed to implant the markers and that new CT and MRI images have to be made after those necessary for diagnosis. As Chapter Two describes, diagnostic workflow for our cases was designed to have CAS-ready CT-scans made, if necessary during the diagnostic process. This was designed to reduce the need for duplicate scans and to lower patient radiation exposure. 3D MRI-only navigation (in contrast to the more common 2D multi-slice MRI fused to a matched CT) is a potential radiation-free alternative with the advances in MRI sensitivity and resolution. Other techniques with fiducial markers like fluoro-CT were also described. If surface matching on MRI is available, fiduciaires are no longer required for (3D) MRI-only navigation. A very interesting, possibly non-invasive future possibility is ultrasound registration through multi-modal matching (53).

There were problems with the navigation systems during procedures, both in the literature and in this thesis. So et al. had two failures on surface registration; the authors believed poor CT and bone quality to be the cause. They switched to fluoro-
CT matching (24). Aponte-Tinao et al. reported three failures, one in software and two in hardware (35). Young et al. had problems achieving an accurate match because of high BMIs and limited exposure in one case and inaccuracies experienced due to a match on a mobile bone segment in another case (28). Chapter Two reported on eight issues with CAS navigation, almost all in the first year of CAS use. In our experience most are related to the learning curve.

There weren’t a lot of specific mentions of high inaccuracy during the procedures (i.e. inaccuracies after a successful match). Young et al. is the only example: they discovered the inaccuracies (due to the match on a mobile segment) only when the hip joint was violated. In Chapter Six we saw some possible inaccuracies that were only detected in post-procedure analysis. Chapter Two describes two non-radical resections in procedures where there was a successful and accurate system setup. A computer navigation system that is mismatched can be highly precise but not accurate, according to the ISO definitions. The only safeguard against these potentially very dangerous hidden inaccuracies is the surgeon. This requires understanding of the systems, method of matching and CAS workflow (continuous checking). It is likely a large part of the clinical learning curve.

As far as we know, there is no mechanism in place that checks match accuracy during the procedure, for example by intermittently checking a known point as a mark on the bone. Redundancy of important systems is standard operating procedure in critical industrial applications of technology, for example in the aviation industry. Currently the only link between spatial and digital anatomical coordinates is the patient tracker. If the tracker is moved relative to the matched bone by mistake, the system accuracy will drop without the surgeon knowing. The same is true for the tools, if a connector moves: the system will still display the point where it is expected to be, not where it actually is. Contact trackers (detect bone contact by means of tools, reconstruct and check surface) or secondary matching mechanisms (3D laser scanning, optical recognition of the bone surface, multi-modal fusion based on ultrasound, etc.) could enable cross-checks to guard against this problem. This will very likely decrease the cognitive load of constantly comparing CAS against surgical intuition. It will also make accepting the objective orientation offered by the system easier, a problem we have especially seen with less CAS-experienced surgeons.

A final argument against the use of CAS or other systems for objective intraoperative navigation was its cost, in terms of (surgical) time and money (43). As Chapter Two demonstrated, surgical set-up time after the initial learning curve can be short. Planning can be done for the most part during patient switches (in anaesthesiology time) or is already required to be done in advance in complex procedures. Chapter Five demonstrated that the CAS workflow does not increase intraoperative time, compensating for the set-up time or even saving time compared to a standard procedure. A CAS system is expensive. However, as Jeys et al. speculated, such
systems can be cost-effective if they reduce complications and local recurrence rates (17). According to a review of Picard et al., it can be cost-effective in standard arthroplasty (54). In addition, use of a CAS system is not limited to orthopaedic oncology.

**Current tools**

The workflow and technique of navigation and instrumentation has changed little since it was first described in 2004 by Hübner et al., who mentioned navigated chisels, and Krettek et al., who used navigated placement of K-wires (21, 22). Optical trackers are still attached to instruments with a binding apparatus, introducing a potential source of inaccuracy. Different instruments have been tracked; some papers describe the use of marking the osteotomy plane with navigated diathermy, drill or bone burr, and perform the resections without navigation support. Others have marked the resection planes on the bone with diathermy, drill holes or K-wires and performed the resection with navigated osteotomes and/or navigated power saws (17).

The need for improved tools can be seen not only in Chapter Six, with the improvements the CAS guide offers over standard CAS – it is also clear in daily practice, with the problems of attaching trackers to instruments and calibrating them, for example in curettage surgery. A major problem addressed in this thesis was that the software and system we use (Orthomap 3D) only offer matching using a calibrator on a 2D point (all instruments are a 2D line). Without direct feedback of orientation of the tool, the surgeon has to interpret this, again relying on an accurate frame of reference. For the placement of the CAS guide we had to rely on two 2D lines to orientate the saw block in a 3d plane, which is not optimal.

In our experience, the use of navigated oscillating saws had a potential drift in accuracy and low precision, whereas other groups have reported successful use of this tool. There are currently no studies available on the accuracy and precision achieved with different instruments or with different CAS systems. In our opinion this information is needed for a better discussion on the application of CAS and for surgical planning.

**Analysis of current use and future perspectives**

**CAS acceptance**

An important aspect of CAS application is the surgical community’s acceptance of the system. In arthroplasty, CAS was first seen as a major revolution by early adopters. However, as Picard et al. state in an article on CAS acceptance in orthopaedic
surgery, acceptance has been slow (54). The use of CAS in orthopaedics may even be decreasing. An important aspect in the acceptance of CAS is likely its image: it is still associated with being a demanding technology, requiring an in-depth technical view, long set-up times and high costs. Still, the interface and workflow of the systems are still aimed at technical users. Significant improvements have been made to the user interface and workflow in the CAS arthroplasty field, but based on our experience the current oncology systems and workflow are not intuitive enough for CAS novices. Investments in the ecosystem and toolsets requires users, and vice versa.

**Current CAS issues**

The current low rate of acceptance can hamper the development of the technique and its ecosystem. Some promising applications of CAS need hardware and software support. In addition to the image-related issues mentioned above, there is only a single registration connection, with no backup system in place to prevent drifts in patient or tool accuracy. The current toolset of an orthopaedic surgeon is not adapted for CAS use, requiring adaptors and often limiting the potential for increased usefulness. Finally, CAS research is still in the phase of case series. We could all benefit from measurement standards for surgical procedures. This would enable comparisons between studies on outcome as well as on modalities and toolsets.

**Current CAS benefits**

CAS can be a technologically superior replacement for fluoroscopy in the curettage of low-grade malignant, intermediate and benign lesions. With adapted tools and software, increases in clinical parameters are very likely. Application of CAS, both in experimental and clinical studies, has shown a very high percentage of radical resections in what are often extremely difficult procedures in the pelvis and long bones. This increase reaches such a degree that a randomised control for high-grade pelvic sarcoma resections may arguably be unethical. The increase in accuracy and precision enables new procedures that wouldn’t have been possible otherwise; this often results in the salvage of critical anatomical structures, thereby drastically improving outcome for our patients. CAS can be used to reconstruct large defects with a high degree of accuracy using grafts and/or (custom) prostheses, enabling more joint salvage surgery and/or increase in patient function. In this thesis CAS set-up time is shown not to be an issue in real-world clinical use. Initiatives for increased accuracy in data reporting have been published in CAS-specific orthopaedic oncology scientific literature and are picking up steam.
Public health benefits

CAS has a role in the current trend in treatment aimed at more limb and joint salvage surgery. In that sense, CAS can improve function, quality of life and the participation in society of patients who were diagnosed with bone cancer. Previously impossible joint salvage procedures are the prime example in this thesis of the effect CAS can have on post-surgical function. However, at this point in time follow-up is not long enough and cohort size not big enough to be able to draw firm conclusions on quality of life and participation. More research is needed on this aspect.

Future perspectives

While CAS in orthopaedic oncology is now more than 10 years old, acceptance has been slow. Technological development will nonetheless continue and will likely accelerate. Complete integration of spatial awareness, advanced imaging possibilities and per-patient reconstructions will completely change the surgical oncology workflow.

In the near future we will see a further integration of our current toolset into the CAS ecosystem, or the development of a separate toolset (e.g. smart burrs or absorption of CAS into robotics). This will increase both the accuracy in the orientation of the tool (no more adapters and 3D depiction of the tools) and the precision of the surgical action. This increased accuracy will mean that we can use more advanced planning software, availing ourselves of virtual surgery simulation tools and physics-based evaluation tools, which will provide a detailed surgical plan. High precision will allow surgeons to adapt procedures to a more efficient balancing of margins versus function. Large defects will be reconstructed using a more patient-specific approach, using 3d printed prostheses or carefully shaped bone grafts. However, even with these smart tools we will be looking at a 2D screen for the next decade.

In the farther future the interface for CAS devices will likely move to an augmented reality approach with an even larger focus on medical imaging. Pre-planning can be done using virtual surgery to evaluate options. It will be possible to make more accurate predictions on the exact level of functioning the patient will have after the surgery based on kinematic models, enabling a data-driven decision process on procedure type and reconstruction, e.g. allograft or custom prosthesis. The patient’s anatomy during surgery is augmented with markers on the points of interest or overlain by the preoperative scans. Low-grade malignant, intermediate and benign lesions will be treated percutaneously. The CAS system will keep track of the position of the bone and instruments in multiple ways, such as multi-modal fusion with ultrasound or 3D (laser) surface detection, ensuring a highly accurate result even when trackers or the robotic connection moves. As high-resolution 3D imaging and overlay headsets are now commonplace, the surgeon can call in
support from other orthopaedic surgeons worldwide. Surgical tools will be semi-autonomous, as passive-smart tools, or fully autonomous after the surgeon holds them to the planning site. The high degree of radical resections with optimal margin will increase the need for early diagnosis even more. Accurate reconstructions will allow postoperative function to be closer to preoperative function, lowering the long-term impact of treatment on orthopaedic oncology patients.
General discussion and future perspectives
References


(28) Young PS, Bell SW, Mahendra A. The evolving role of computer-assisted


