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AUGMENTED NAVIGATION

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Augmented Navigation

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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To my family

I hear, and I forget.

I see, and I remember.

I do, and I understand.

- Xúnzǐ c. 310 – c. 235 BC

ABSTRACT

Spinal fixation procedures have the inherent risk of causing damage to vulnerable anatomical structures such as the spinal cord, nerve roots, and blood vessels. To prevent complications, several technological aids have been introduced. Surgical navigation is the most widely used, and guides the surgeon by providing the position of the surgical instruments and implants in relation to the patient anatomy based on radiographic images. Navigation can be extended by the addition of a robotic arm to replace the surgeon's hand to increase accuracy. Another line of surgical aids is tissue sensing equipment, that recognizes different tissue types and provides a warning system built into surgical instruments. All these technologies are under continuous development and the optimal solution is yet to be found. The aim of this thesis was to study the use of Augmented Reality (AR), Virtual Reality (VR), Artificial Intelligence (AI), and tissue sensing technology in spinal navigation to improve precision and prevent surgical errors.

The aim of Paper I was to develop and validate an algorithm for automatizing the intraoperative planning of pedicle screws. An AI algorithm for automatic segmentation of the spine, and screw path suggestion was developed and evaluated. In a clinical study of advanced deformity cases, the algorithm could provide correct suggestions for 86% of all pedicles—or 95%, when cases with extremely altered anatomy were excluded.

Paper II evaluated the accuracy of pedicle screw placement using a novel augmented reality surgical navigation (ARSN) system, harboring the above-developed algorithm. Twenty consecutively enrolled patients, eligible for deformity correction surgery in the thoracolumbar region, were operated on using the ARSN system. In this cohort, we found a pedicle screw placement accuracy of 94%, as measured according to the Gertzbein grading scale.

The primary goal of Paper III was to validate an extension of the ARSN system for placing pedicle screws using instrument tracking and VR. In a porcine cadaver model, it was demonstrated that VR instrument tracking could successfully be integrated with the ARSN system, resulting in pedicle devices placed within 1.7 ± 1.0 mm of the planed path.

Paper IV examined the feasibility of a robot-guided system for semi-automated, minimally invasive, pedicle screw placement in a cadaveric model. Using the robotic arm, pedicle devices were placed within 0.94 ± 0.59 mm of the planned path. The use of a semi-automated surgical robot was feasible, providing a higher technical accuracy compared to non-robotic solutions.

Paper V investigated the use of a tissue sensing technology, diffuse reflectance spectroscopy (DRS), for detecting the cortical bone boundary in vertebrae during pedicle screw insertions. The technology could accurately differentiate between cancellous and cortical bone and warn the surgeon before a cortical breach. Using machine learning models, the technology demonstrated a sensitivity of 98% [range: 94-100%] and a specificity of 98% [range: 91-100%].

In conclusion, several technological aids can be used to improve accuracy during spinal fixation procedures. In this thesis, the advantages of adding AR, VR, AI and tissue sensing technology to conventional navigation solutions were studied.

LIST OF SCIENTIFIC PAPERS

I. Machine learning for automated 3-dimensional segmentation of the spine and suggested placement of pedicle screws based on intraoperative cone beam computer tomography
Burström G, Buerger C, Hoppenbrouwers J, Nachabe R, Lorenz C, Babic D, Homan R, Racadio J, Grass M, Persson O, Edström E, Elmi-Terander A.
J Neurosurg Spine, 2019 Mar 22, 31(1):147-154.

II. Pedicle screw placement using augmented reality surgical navigation with intraoperative 3D imaging: a first in-human prospective cohort study
Elmi-Terander A*, **Burström G***, Nachabe R, Skulason H, Pedersen K, Fagerlund M, Ståhl F, Charalampidis A, Söderman M, Holmin S, Babic D, Jenniskens I, Edström E, Gerdhem P.
Spine (Phila Pa 1976), 2019 Apr 1, 44(7):517-525.

III. Augmented and virtual reality instrument tracking for minimally invasive spine surgery: A feasibility and accuracy study
Burström G, Nachabe R, Persson O, Edström E, Elmi-Terander A.
Spine (Phila Pa 1976), 2019 Aug 1, 44(15):1097-1104.

IV. Feasibility and accuracy of a robotic guidance system for navigated spine surgery in a hybrid operating room: a cadaver study
Burström G, Balicki M, Patriciu A, Kyne S, Popovic A, Holthuizen R, Homan R, Skulason H, Persson O, Edström E, Elmi-Terander A.
Scientific Reports, 2020 May 5;10(1):7522.

V. Diffuse reflectance spectroscopy accurately identifies the pre-cortical zone to avoid impending pedicle screw breach in spinal fixation surgery
Burström G, Swamy A, Spliethoff J, Reich C, Babic D, Hendriks B, Skulason H, Persson O, Elmi-Terander A, Edström E.
Biomedical Optics Express, 2019 Oct 24, 10(11): 5905-5920.

CONTENTS

LIST OF ABBREVIATIONS

3D	3-Dimensional
AR	Augmented Reality
ARSN	Augmented Reality Surgical Navigation
CBCT	Cone Beam Computed Tomography
CT	Computed Tomography
DRF	Dynamic Reference Frame
DRS	Diffuse Reflection Spectroscopy
FH	Freehand
HMD	Head-Mounted Display
MISS	Minimally Invasive Spine Surgery
MRI	Magnetic Resonance Imaging
OR	Operating Room
OTS	Optical Tracking System
SVM	Support Vector Machine
VR	Virtual Reality

1 INTRODUCTION

Modern spine surgery still relies significantly on the knowledge and manual skills of the surgeon. Even though the outcome of the surgery depends on the performance of the individual surgeon and the team in the operating room (OR), the procedure also extends outside the OR. The process begins when a patient is first evaluated, and data from labs, physiotherapists and occupational therapists, and preoperative imaging such as computed tomography (CT) and magnetic resonance imaging (MRI) is aggregated. Based on a synthesis of the information gathered preoperatively, the experienced surgeon makes a judgment on whom to operate and how. This synthesis of information should ideally carry over into the OR for the best surgical outcome. Despite these preparations, however, spine surgery includes manipulation of complex and dynamic 3D structures, and human errors do occur. Having access to relevant imaging data in the OR is a common way of minimizing the risk of surgeon-based errors. Radiological imaging data can be provided on printouts, old-fashioned X-ray display cabinets, or monitors or through customized 3D-printed models accessible in the OR. Increasingly, the intraoperative setup is supplemented by computer-aided surgical navigation systems in an effort to provide relevant surgical information to the surgeon for optimal surgical outcomes. In this thesis, the aim is to introduce the forefront of technological aids used in spine surgery and to present a unique contribution to the field via the study of technological aids that all strive to improve accuracy and reduce surgical errors during spine surgery.

In the following two sections of the introduction, readers previously unfamiliar with spine surgery are introduced to the historical background and basic concepts of spine surgery. For readers already familiar with the field of spine surgery or spine research, section 1.3 will serve as the introduction to the specific concepts of navigated spine surgery.

1.1 HISTORICAL BACKGROUND

The history of spine surgery extends to the early beginnings of medicine. The first known description of ailments relating to the spinal column and its treatments can be found in the *Edwin Smith papyrus*, written sometime after 1700 BC during the time of the New Kingdom in Egypt (7). In the document, five cases of traumatic spinal injury were described. Those with paralysis were left untreated, while those without neural injury received wound dressings and fixation in a prone position. Later, in the works of Hippocrates (460–370 BC) and the Hippocratic School, numerous spinal ailments were described; the preferred treatment options were external stabilization and immobilization (7, 8). The first historical record to advocate for surgical intervention was the works of Galen of Pergamon (129–200 AD), who—besides coining the terms *kyphosis, lordosis,* and *scoliosis*—recommended the removal of fractured bone fragments pressing into the spinal canal. Particularly interesting for the topic of this work are the works of Paul of Aegineta (625–690 AD), who was not only the first to describe and recommend laminectomy for laminar fractures with cord compression but also designed several surgical instruments (elevators, bone biters, and raspatories), which are perhaps the first detailed accounts of technological aids used for spine surgery (7, 8).

However, only in the 1970s did spine surgery truly experience widespread adoption. This culmination occurred after multiple innovations in surgical techniques and implants, including Dandy's pneumomyelography in 1919, Harrington's proposition of dorsal instrumentation for correcting scoliosis in 1958, Oroczco's and Llovet's use of plates for securing bone chips in 1970, and Hounsfield's computed tomography (CT) in 1971 (8, 9). Adding lateral radiographs to the surgeon's use of intraoperative anatomical landmarks formed the initial step toward navigation and increased surgical accuracy in spine surgery (10-12). The first technical aid in spine navigation was 2D fluoroscopy (13). Since then, image-guided and minimally invasive technologies have successfully been applied to spinal surgery (14). Over the past 30 years, there has been a rapid evolution of technical solutions for navigation in general. Fluoroscopy has been replaced with 3D-imaging techniques, and intraoperative imaging has supplanted preoperative imaging in many situations (14). These, as well as numerous other important discoveries and innovations, have led to the worldwide development of spinal procedures as they are known today.

1.2 BASIC CONCEPTS IN SPINE SURGERY

1.2.1 Spinal anatomy

The human spine consists of a set of bones and their associated discs and ligaments. The bone structure entails 32–34 vertebrae, including seven cervical vertebrae (C1-C7), 12 thoracic vertebrae (Th1–Th12), five lumbar vertebrae (L1–L5), five sacral vertebrae (S1–S5), and three to five coccygeal vertebrae (Figure 1)(15). The sacral vertebrae typically fuse to form the sacrum, and the coccygeal vertebrae fully or partially fuse to form the coccyx (15). The anatomy of a vertebra varies between levels; however, principally, each vertebra consists of a vertebral body, a vertebral arch, and vertebral processes (Figure 2)(16-18).

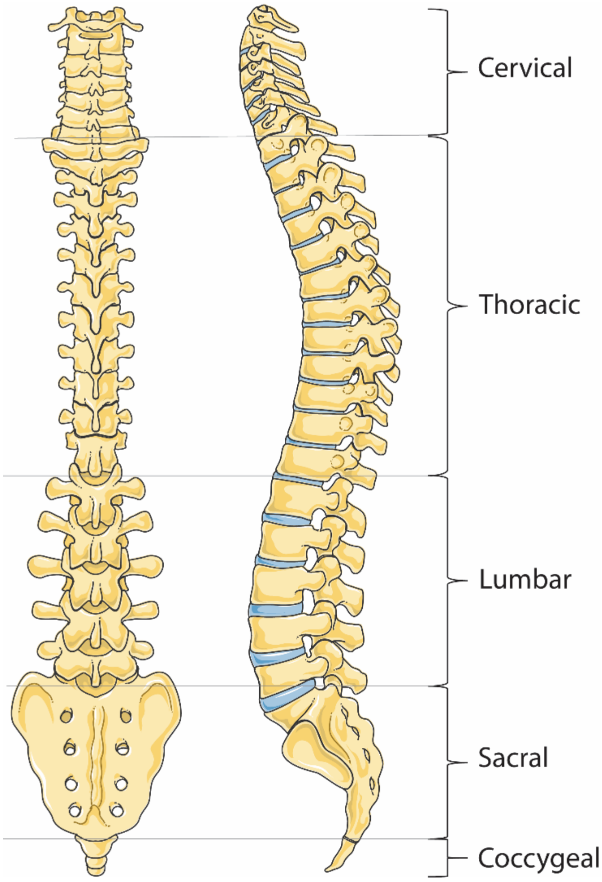

Figure 1. Anatomy of the spinal column. To the left, posterior view. In the middle, anterior view. To the right, lateral view. Illustration adapted from Servier Medical Art under CC attribution license 3.0.

A vertebral arch consists of two pedicles, connecting the vertebral body with the posterior parts of the vertebrae, and the lamina (Figure 2). The spinal canal contains the spinal cord, fat, blood vessels, and ligaments. Under each of the pedicles (or above, according to the convention of counting in the cervical spine), the spinal nerves leaves the spinal cord and passes through the intervertebral foramina, branching out to the rest of the body.

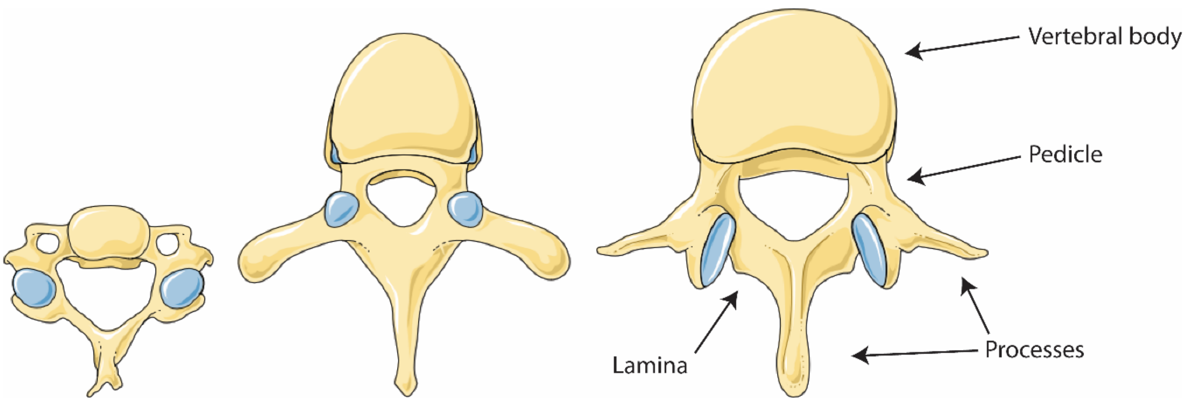

Figure 2. Vertebral anatomy. To the left, a cervical vertebra. In the middle, a thoracic vertebra. To the right, a lumbar vertebra. Illustration adapted from Servier Medical Art under CC attribution license 3.0.

1.2.2 Spinal fusion surgery

Spinal surgical procedures encompass numerous interventions ranging from the stabilization of acute traumatic injuries to surgical removal of tumors (19). The spine procedure that has received the most attention of technological aids, however, is the placement of pedicle screws (20, 21). This is likely due to the combination of recurring surgical errors and the availability of potential technical solutions to prevent those errors. The basic concept of spinal fusion surgery employs surgical techniques in which two or more vertebrae are fused using screws, rods, and sometimes hooks (together called spinal instrumentation) and bone graft material (22, 23). The purpose of spinal fusion is to eliminate motion between the affected vertebrae either to reduce pain (for degenerative indications) or to improve the stability of the spine (for traumatic and deformity indications) (22, 23). In its simplest form, a spinal fusion of two levels consists of placing screws inside each pedicle (called pedicle screws, see Figure 3) that extend into the vertebral bodies of both vertebrae to be fused (i.e., two pedicle screws per vertebra). These are attached using rods to create a rigid connection between the two vertebrae (24). At certain levels or for traumatic or anatomical variations, other forms of screw or hook placement can be used, especially in the cervical region where possible variations are numerous, depending on the specific level.

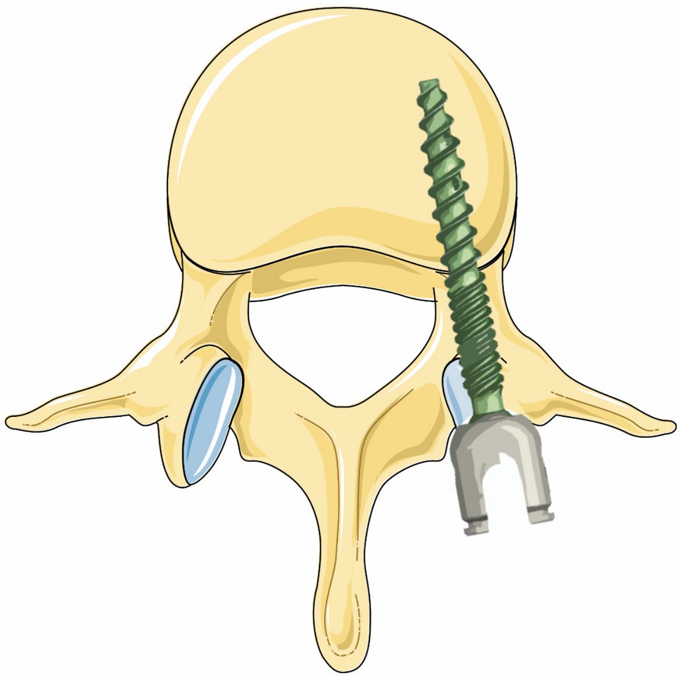

Figure 3. Lumbar vertebra with pedicle screw. Green part of pedicle screw illustrated intra-vertebral part. Illustration adapted from Servier Medical Art under CC attribution license 3.0.

The accurate placement of pedicle screws in fixation surgeries is essential to avoid vascular and neural injuries as well as reoperations (25, 26). Meta-analyses have reported varying but significant pedicle screw accuracy rates. Kosmopoulos and Schizas reported pedicle screw accuracies ranging from 60% to 97.5% in the lumbar spine and from 27.6% to 96.5% in the thoracic spine when surgery is performed using the freehand (FH) technique (27). In a study looking at reoperation rates after pedicle screw placement, Staartjes and colleagues found that 3.3% of pedicle screws placed using FH required revision surgery (28). Thus, pedicle screw placement using conventional methods needs to be improved.

Computer-assisted navigation was initially promoted to ensure the correct level was operated upon (9, 29). As the technology has matured, research has primarily focused on the precise placement of pedicle screws to avoid complications (20, 30, 31). It is now the most investigated technology for reducing pedicle screw complications (31). Similarly, the introduction of robots in spinal surgical procedures was primarily aimed at minimizing the frequency of wrongly placed pedicle screws (28, 32). A third modality for preventing pedicle screw breaches was the introduction of tissue-sensing surgical instruments. In this method, the surgeon receives direct feedback about the tissue type located at the tip of the instrument. To date, there is only one commercially available product, relying on electrical conductivity to indicate its proximity to the cortical bone wall (33, 34).

1.3 COMPUTER-ASSISTED SURGERY

Computer-assisted surgery (CAS) is an umbrella term for multiple technologies aiming to improve surgical outcomes, but it is most often used to refer to surgical navigation systems. For the sake of consistency, the term “surgical navigation” will be used throughout this thesis to refer to the use of computer-assisted surgery and navigation.

Surgical navigation consists of a system that provides a real-time display of the current position of instruments in relation to anatomical structures in the surgical field (35, 36). Most spinal navigation systems rely on a frameless stereotactic approach where the patient is typically tracked using optical markers on a dynamic reference frame (DRF) that is firmly attached to the bone (37). The concept was developed for applications in cranial surgery in the 1990s and has experienced nearly universal adoption in the field throughout most middle- and high-income countries (38). However, optimization of spinal applications has not enjoyed the same quick development and adoption (13). The underlying reasons for this lack of adoption have been attributed both to the technical challenges unique to the spine, as well as a perceived low benefit-to-disadvantage ratio of commercially available solutions (13, 39). Specifically, high costs, lack of available equipment, and perceived increases in OR time are commonly cited as reasons for not using surgical navigation (13). In cranial navigation, the reference frame is attached to one rigid bony structure; in the spine, there are 25 semi-independent vertebral bones to be tracked (treating the sacrum as one bone and excluding the coccyx). While there is no movement of structures between imaging and the start of surgery in cranial applications, the spine moves considerably, requiring intraoperative imaging or computed correction of preoperative radiology to sustain the accuracy (40-42).

1.3.1 Components of a surgical navigation system

Surgical navigation systems need patient imaging for displaying anatomical positions

Since spinal navigation either requires intraoperative imaging or preoperative imaging with intraoperative updates, several commercial solutions have been presented. Over time, these solutions have relied on an increasingly sophisticated underlying technology. In principle, the solutions can be divided into four main groups:

I. Intraoperative 2D fluoroscopic navigation
II. Preoperative CT/MRI with manual intraoperative registration
III. Preoperative CT/MRI with fluoroscopic registration and update
IV. Intraoperative CT or CBCT with or without fusion to preoperative MRI

Intraoperative 2D fluoroscopic navigation relies on an intraoperative C-arm to obtain AP (i.e., coronal) and lateral (i.e., sagittal) views for navigation. It was introduced in the early 2000s. The main advantage over regular fluoroscopy is that the procedure provides fully automatic registration and reduction of radiation to the staff (43). However, the lack of axial imaging is considered a major limitation (39).

Preoperative CT/MRI with manual intraoperative registration was introduced in the late 1990s as a direct extension of cranial navigation (39). As with cranial applications, the preoperative CT or MRI images are manually registered intraoperatively using surface-based registration. Since each vertebra can move semi-independently, all vertebras to be operated on need individual registration. Nottmeier and colleagues found the average registration time per vertebra was approximately two minutes, and 13% of vertebrae required re-registration (44). This time-consuming procedure is one of the key reasons for the limited adoption of surface-based registration of preoperative CT/MRI imaging in the field of spine surgery (39).

Preoperative CT/MRI with fluoroscopic registration and updating relies on combining preoperative 3D data with automatic intraoperative registration using anterior-posterior and lateral fluoroscopic images. This leads to a semi-automatic registration of the preoperative 3D data, without the time-consuming workflow of manual surface registration.

Figure 4. Intraoperative cone-beam computed tomography (CBCT). Intraoperative setup representing an example of intraoperative CBCT (to the left, grey) used with a surgical navigation system.

Lastly, intraoperative CT/CBCT relies on conventional intraoperative 3D imaging coupled to a reference marker, which is attached to the patient in or around the surgical field to allow for patient registration and tracking. An example of the intraoperative CBCT setup is illustrated in Figure 4. These systems currently represent state-of-the-art technology in spinal navigation while also incurring high costs for hospitals (45, 46). Although there are several commercially available intraoperative MR solutions, no reports on the use of intraoperative MR for spinal navigation have been published at present. This may be due to the time-consuming and complex process of intraoperative MR imaging, including the need for MR-compatible instruments and substantial training of the OR staff.

Continuous tracking of the patient and instruments is needed to compensate for movement

For navigation to work, the 3D imaging must be co-registered to the patient's position in the OR and continuously tracked by the navigation system to compensate for movements during surgery (47). While different tracking solutions have been employed, the principal technology is essentially unchanged. For tracking the patient, a DRF is typically used, which is comprised of a star-shaped metal frame firmly attached to an index vertebra and equipped with multiple optical spheres that are recognized by an infra-red (IR) camera (Figure 5). Similar reflective spheres serve as trackers on surgical instruments or pointers that can display their position relative to the patient's anatomy. This information is presented to the surgeon on monitors as virtual objects overlaid on the patient's 3D imaging (47-53).

Figure 5. Depiction of a dynamic reference frame used for tracking the patient, during minimally invasive surgery. Photo reproduced with permission from He et al (5).

Efforts have been made to design patient-tracking methods based on unobtrusive markers or no markers at all. An alternative solution is to rely on an optical tracking system (OTS), consisting of high-resolution video cameras at different angles around the surgical field. The system primarily used in this thesis uses this solution, in which cameras are embedded in the flat-panel X-ray detector of a motorized C-arm (54). Flat adhesive skin markers, randomly placed around the surgical field, are tracked by the video cameras (54-58). The OTS uses triangulation and creates a 3D point pattern based on the individual markers' relative positions to each other (59, 60). The relation between the OTS and the intraoperative CBCT coordinates is known based on initial manufacturing calibrations. Therefore, CBCT coordinates can be converted to OTS coordinates and vice versa.

An alternative tracking method, employed in several AR systems, consists of direct surface tracking using visible anatomical features such as the skin or exposed internal anatomy (61-66). In current systems, however, hand gestures are first used to align the 3D imaging manually with the surgical view of the vertebrae. This introduces a significant risk of misalignment if the user is not meticulous. The system relies on surface tracking to keep the image in the correct position. Current research developments are moving toward systems that automatically identify surface anatomy and correlate it with the preoperative or intraoperative imaging so that the patient and 3D imaging can be automatically aligned (67-69).

1.3.2 Conventional surgical navigation

Since surgical navigation systems have existed for more than 20 years in clinical practice, a typical generic setup has evolved that is used by numerous manufacturers (70-72). This thesis collectively calls these systems “conventional navigation” to separate them from alternate technical solutions that have been presented in recent years, some of which are being studied here. Conventional spinal navigation typically consists of a DRF firmly attached to the spinous process of the vertebrae to be operated on and tracked by a set of infra-red cameras. In addition, surgical instruments (e.g., drills or awls) or custom pointers are usually tracked. The information is presented on a monitor, displaying preoperative or intraoperative imaging in axial, sagittal, and/or inline coronal planes. In this design, the surgeon has two different areas of focus during surgery—the surgical area and the separate navigation monitor. All translation of information from one to the other occurs in the surgeon’s mind.

Conventional navigation has been extensively studied for its use in pedicle screw placement. When compared to the FH approach, several meta-analyses have found the use of conventional navigation to be superior (27, 28, 73, 74). Kosmopoulos and Schizas reported the median screw placement accuracy using navigation was 95.2% compared to 90.3% when using FH (27). In a more recent meta-analysis looking at the need for revision surgery due to pedicle screw misplacement, Staartjes and colleagues found that 0.9% of pedicle screws placed with navigation required revision surgery, compared to 3.3% placed with FH (28).

Studies comparing different surgical navigation technologies are fewer than those comparing a specific navigation method to the FH technique. In the largest meta-analysis to date by Du and colleagues, intraoperative 3D image-based navigation was found to provide superior accuracy over 2D fluoroscopic navigation and preoperative 3D image-based navigation with manual registration (46).

1.3.3 Augmented reality navigation

Augmented reality (AR) navigation has drawn increased scientific interest in recent years (54, 56, 62, 75). Its main difference from traditional surgical navigation systems lies in the interface presented to the surgeon. Instead of presenting the navigation view as animated surgical instruments superimposed over CT/MRI images in standard anatomical views, AR navigation typically provides a real-world view (video or actual) of the surgical area with overlays of animated surgical guides (76). Such animated guides can either highlight the deep anatomy superimposed over the patient’s skin or consist of animated trajectories highlighting optimal tool placement (54, 56, 62). The main point of AR is to remove the need for shifts of focus during surgery (between the surgical area and navigation monitor) that are otherwise necessary for image-guided navigation.

AR navigation systems can be further divided into four main types:

I. Monitor-based augmented reality
II. Microscope-based augmented reality
III. Holographic augmented reality
IV. AR navigation using a head-mounted display (HMD)

The monitor-based AR navigation systems provide a video view of the surgical area while superimposing information over this view. Since the position of the video camera is known and stationary, the accuracy of the superimposed information is high (52, 54, 56, 77). However, surgeons are confined to looking at a monitor instead of the actual surgical area. Meanwhile, AR navigation using an HMD places both a video camera and a display on the head of the surgeon. The video camera provides a video feed from the same perspective as the surgeon's, while the video display is typically a see-through display used for superimposing information in the surgeon's field of view (62). Currently, one commercially available product for clinical use exists on the market, Augmedics xvision (Arlington Heights, IL, USA). In addition, a general HMD device—Microsoft HoloLens (Redmond, WA, USA)—has also been adapted for use in spine surgery. Both have been extensively studied preclinically (52, 53, 61-63, 78, 79).

Direct comparative studies between AR-navigation systems and conventional image-guided navigation are rare in the scientific literature. In one study, Müller and colleagues used an HMD-AR device to place pedicle screws (53). The control group consisted of patients treated with a widely conventional navigation system. There were no significant differences in translational errors (AR: 3.4 ± 1.6 mm vs PTS: 3.2 ± 2.0 mm, $p = 0.85$). Reviews highlighting the potential benefits of AR over traditional surgical navigation systems have mentioned ease-of-use and workflow improvements while identifying accuracy as the most pressing technical challenge (62, 75, 80).

Direct comparisons between different AR interfaces are lacking, likely owing to the preclinical nature of most setups and studies and the novelty of the technology. When comparing the reported registration accuracies between HMD and monitor-based AR, the latter consistently yields lower errors (52, 62, 77). This reflects the technical challenge of adding an extra dimension to the tracking setup (i.e., with a non-stationary field of view).

1.4 ROBOT-ASSISTED SURGERY

Perhaps a natural continuation of surgical navigation systems, the addition of a robotic arm to the navigation system has the premise of providing higher accuracy. Several navigated robotic systems are currently available. They employ different solutions for 3D planning, using either preoperative or intraoperative CT imaging, with or without intraoperative fluoroscopy. Among the most well-published ones are the ROSA Spine system (Medtech S.A., Montpellier, France) and the Mazor robots (Renaissance Guidance System and SpineAssist, MAZOR Robotics Ltd., Caesarea, Israel) (21, 76, 81). In the ROSA system, intraoperative fluoroscopy or CT supports the 3D planning. The system employs a navigation camera and reference markers attached both to the patient and to the robot, allowing real-time patient and instrument tracking (82, 83). The Mazor robots rely instead on merging the preoperative CT and 3D planning with intraoperative fluoroscopy updates (84, 85). Both systems uses a robotic arm for instrument guidance (86).

Reviews on robot-guided surgery have concluded that the technology consistently yields a non-inferior accuracy when compared to fluoroscopy-based techniques (32, 86). However, one recent randomized study indicated superior accuracy for robot guidance (87). Effects on length of hospital stay, radiation exposure, and operative time remain uncertain (28, 32, 86, 88). Nonetheless, innovation and the pace of product releases seem to be increasing in the field. Until 2017, only one manufacturer of spine robots (Mazor Robotics) had FDA clearance for two of its systems, SpineAssist and Renaissance Guidance System. Since then, three more manufacturers have received FDA clearance, namely the ExelsiusGPS (Globus Medical Inc., Audubon, PA, USA), Cirq (Brainlab AG, Munich, Germany), and ROSA One (Zimmer Biomet, Warsaw, IN, USA).

1.5 TISSUE SENSING TECHNOLOGY

Tissue sensing technologies, sometimes referred to as sensing instruments, represent a fundamentally different approach to improved spine surgical safety than navigation and robotic aids. Instead of improving the spatial information for surgeons, tissue sensing technologies provide a "sixth sense" by enabling tissue characterization at the tip of surgical instruments. In doing so, for example, the cortical border of vertebrae can be identified by the instrument. It can both be a stand-alone solution for improving accuracy in spine surgery irrespective of the surgical method, as well as a supplementary technology to navigation and robotics via an additional layer of assurance in case of navigation errors.

The idea of sensing tissues is not radically different from common methods in spine surgery today that detect misplaced implants. Conventional breach detection methods involve simple tactile feedback using pedicle probes and neurophysiological monitoring (electromyography, EMG), including electrical stimulation of the pedicle screws after placement in order to detect any direct contact with nerve roots (89). Similar technologies can also provide electrical stimulation of the pilot hole even before placing the pedicle screw in order to avoid potential early injury (90, 91). These methods may help in identifying pedicle breaches but have not sufficed in reducing pedicle screw misplacements rates to acceptable levels, as they are frequently part of the routine in FH series that newer technologies aim to improve upon (27).

1.5.1 Electroconductive sensing

Representing the most widely published approach for enabling tissue sensing technology to detect the cortical border in spine surgery, electroconductive sensing has low-grade evidence for use in pedicle screw placement (34, 92, 93). It is commercially available in the form of a pedicle cannulation device, the PediGuard (SpineGuard SA, Vincennes, France). The technology relies on measuring the electrical conductivity at the sharp tip of the instrument while cannulating the pedicle. The measured conductivity is translated into an audible sound and by a LED light, to inform the surgeon of when changes occur at the tip. Providing the highest grade of evidence to date, Ovadia and colleagues retrospectively compared 98 pediatric patients operated on using an electroconductive sensing device to a matched cohort of 248 pediatric patients operated on using the FH approach (93). They found that the share of patients with neuromonitoring alarms was 6.6% in the FH group versus 3.0% in the electroconductive-sensing device group. This indicates that the tissue sensing technology might decrease the number of clinically relevant screw misplacements, but the technology has yet to be validated in higher quality studies.

A potential drawback of using electrical conductivity is that the technology lacks direction. If, for example, the instrument tip is close but parallel to cortical bone, the technology will still provide a warning. Similarly, even if it correctly detects an impending pedicle screw breach, the surgeon still does not know in what direction the breach is about to happen since the measurement occurs in all directions simultaneously (33). This means that when the device gives a warning, the surgeon must determine how to adapt the next attempt without directional input.

1.5.2 Optical sensing

Optical technologies potentially allow for direct optical measurement of the tissue surrounding an instrument. Unlike electroconductive sensing, a light cone has a specified direction. When employing a forward-looking light cone, the system has the potential to give a warning only if the cortical border is directly in front of the instrument, ignoring cortical walls running parallel to the probe. A probe with multiple light cones in different directions could even provide maneuvering feedback to the surgeon, indicating how the screw path should be corrected in order to avoid a breach. So far, however, no optical technology has been validated for use in spine surgery.

A potential candidate technology called Raman spectroscopy, which works by illuminating tissues using a laser, has previously been used to assess bone quality both transcutaneously and invasively (94, 95). However, Raman spectroscopy is known for long acquisition times due to the low share of light undergoing the necessary interactions with the probed tissue. Typically, acquisition times are one or two orders of magnitude higher than other optical spectroscopic methods, yielding a less-feasible alternative when direct feedback is necessary (96, 97).

Diffuse reflectance spectroscopy (DRS) is an optical sensing technology that has been previously investigated primarily for discriminating healthy tissues from tumor tissues in liver, colon, brain, lung, and breast applications (98-110). It has recently been adapted and applied, through Monte Carlo simulations, to discriminate between cancellous and cortical bone (111). However, it has not yet been validated in real tissues or in a surgical setting. The technology relies on illuminating tissues with white light from a broad-spectrum light source, using optical fibers. When illuminating the tissue, the light is either absorbed, reflected, or scattered. This constitutes a diffuse reflectance pattern, hence the term diffuse reflectance spectroscopy. The diffusely reflected light is then returned through a separate optical fiber and analyzed for spectral changes (112). These changes originate from highly specific absorption, reflection, and scattering characteristics of individual tissue types (113). It has previously been demonstrated that it is possible to estimate the fraction of blood, lipids, and collagen, and a number of other constituents, by applying trained machine learning algorithms to the spectral curves (100, 106, 112-118). Thus, different tissue types can be distinguished by analyzing the reflected light (115). In spinal fixation surgery, DR spectroscopy employed at the tip of surgical instruments could potentially provide real-time feedback to surgeons regarding what tissue type that the instrument encounters.

2 AIMS

The overall aim of this thesis was to increase pedicle screw placement accuracy during spinal fusion surgery by investigating the impact of several technological solutions, and to reduce potential drawbacks on workflow when these solutions are used in the OR. The specific aims of each constituent paper were as follows:

I. Automating procedural steps in surgical navigation can increase accuracy and safety while saving valuable OR time. The aim of **Paper I** was to develop, and to study the accuracy and clinical validity of a technology designed for automatic pedicle identification and pedicle screw trajectory suggestion.

II. Surgical navigation using augmented reality has an advantage compared to conventional navigation by integrating the navigational information in the view of the surgical field. In **Paper II**, the aim was to evaluate the accuracy of pedicle screws placed using augmented reality surgical navigation.

III. Adding instrument tracking based on virtual reality to augmented reality surgical navigation could improve accuracy by promoting adherence to the surgical plan. In **Paper III**, the aim was to study the accuracy and feasibility of adding instrument tracking to the augmented reality surgical navigation system.

IV. Pedicle screw placement accuracy relies on the accuracy of the co-registration of the patient to the image, the correct tracking of the patient and instruments, and the adherence to the planned path by the surgeon. The use of a surgical robot could reduce manual surgical errors. In **Paper IV**, the aim was to study the feasibility and accuracy of integrating a surgical robot with the augmented reality surgical navigation system.

V. Image-guided navigation is one way of reducing surgical errors during pedicle screw placement. A warning system for an impending cortical breach based on tissue sensing is another potential solution. In **Paper V,** the aim was to build and validate a DRS-based feedback system for prevention of pedicle screw breach in a surgical setting using typical breach scenarios.

3 BRIEF SUMMARY OF MATERIALS AND METHODS

An in-depth description of the materials and methods used in the constituent papers is found in each article. In the following text, a summary of the most important concepts used in this thesis is presented.

3.1 AUGMENTED REALITY SURGICAL NAVIGATION (ARSN)

The studies using augmented reality surgical navigation (ARSN, **Papers I-V**) were conducted in a hybrid OR equipped with a radiolucent, motorized, carbon-fiber surgical table connected to a robotic ceiling-mounted C-arm system (AlluraClarity Flexmove, Philips, Best, the Netherlands). The ARSN system has been extensively described in previous studies (4, 54, 56). The system was based on video input from four optical cameras mounted into the frame of the C-arm detector (Figure 6, left). Patient tracking was ensured by continuous video detection of flat, adhesive circular markers placed on the surface around the surgical field. The C-arm enabled 3D cone-beam CT (XperCT, Philips, Best, the Netherlands) scans for planning screw placement and confirming proper screw position. The vertebrae and corresponding pedicles were automatically segmented on the planning CBCT scan. A screw entry was suggested for each vertebra, but the final placement was always actively performed by the surgeon. Screw dimensions (i.e., width and length) were always specified by the surgeon. The intraoperative CBCT and the planned paths for screw placement were augmented to the video images showing the surgical field. The screws are navigated to the desired location by following the planned path displayed on a medical-grade monitor (Figure 6 right).

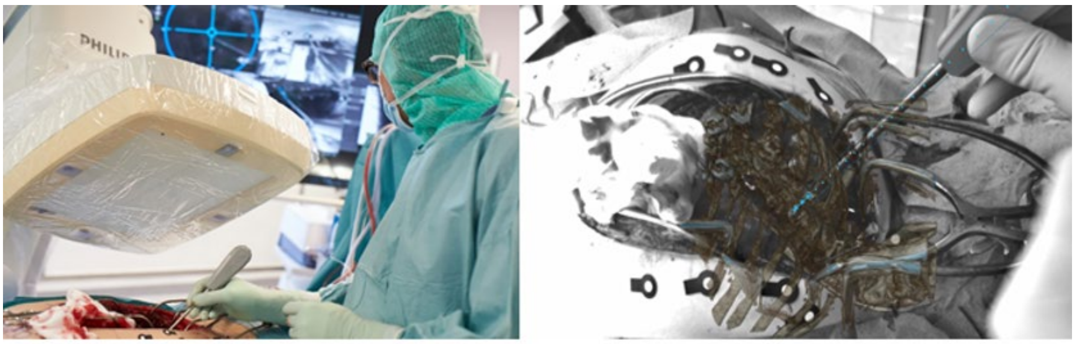

Figure 6. Augmented reality surgical navigation (ARSN). In the left photo, the C-arm detector is visible to the left and includes 4 cameras. Surgical monitor with AR overlays visible in background. In the right photo, surgical view including AR guidance in blue.

3.2 ROBOTIC ARM INTEGRATED WITH ARSN

In **Paper IV**, a robotic arm was integrated with the ARSN system. The robot was lightweight (7 kg) and directly mounted on the OR table (Figure 7). The system automatically aligned the elected instrument according to the surgical plan using only instrument-tracking feedback. The levels to be treated were identified by fluoroscopy, and the robot was mounted on the table rail system. Because of the integration with ARSN, no calibration was needed before the start of surgery. The robot arm had five motorized axes used for positioning instruments in three translations and two angles of rotation for positioning straight instruments like needles and drills. An integrated force-torque sensor was used to measure loads on the instrument guide. This enabled force control of the robot, offering a “passive mode” where the surgeon steered the robot by directly pushing or pulling on the instrument guide. The robot was primarily controlled remotely via a gaming-type controller. This allowed it to move autonomously at the click of a button due to the integration of the surgical navigation system and the predefined pedicle screw trajectories. The instrument guided the robot-accepted adapters for standard surgical instruments, such as drills, Jamshidi needles, and pedicle probes.

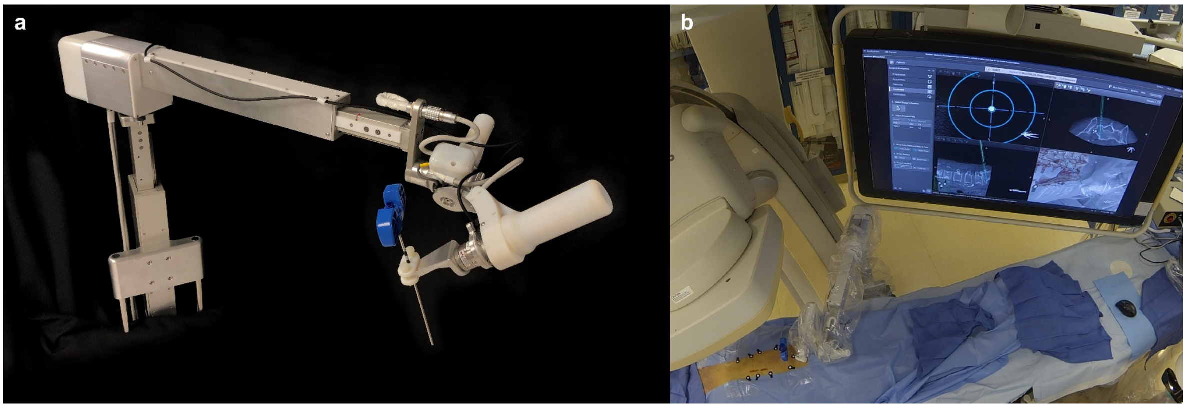

Figure 7. Robot arm. In (a), the robotic arm including mounted Jamshidi needle (blue). In (b), the surgical setup including surgical navigation monitor. Figure republished with permission, original work by Burström et al (1).

3.3 GERTZBEIN GRADING

The Gertzbein grading system is an accuracy scale for pedicle screw placement that is widely used in the field (119). It grades each screw in a four-step fashion. The original scale included six grades, but the higher-inaccuracy grades were largely abandoned in later studies. In the present studies, the implementation of the Gertzbein grading was defined as follows: grade 0 (screw entirely within pedicle), grade 1 (breach < 2 mm), grade 2 (breach 2 – <4 mm), and grade 3 (breach ≥ 4 mm), as shown in Figure 8. In our studies, accuracy was defined as combined grade 0 and grade 1. In this thesis, as is common in the field, accuracy according to the Gertzbein grading is referred to as “clinical accuracy” as opposed to “technical accuracy”, where deviations from targets are measured in millimeters. Note however, that the use of “clinical accuracy” still refers to a radiological assessment.

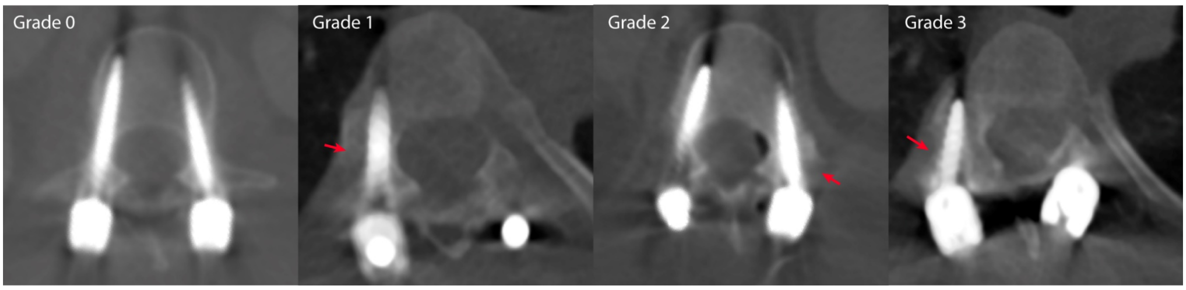

Figure 8. Gertzbein grading scale. From left to right, the illustration is showing: grade 0 (screw entirely within pedicle), grade 1 (breach < 2 mm), grade 2 (breach 2 – <4 mm) and grade 3 (breach ≥ 4 mm). Figure republished from Burström et al (120), licensed under CC attribution 4.0 license (http://creativecommons.org/licenses/by/4.0/).

3.4 TECHNICAL ACCURACY

The term technical accuracy refers to the absolute accuracy of a placed pedicle device in millimeters in relation to the planned path. The value given was the error distance (in mm) between the intended target and the actual pedicle screw placement. By definition, in order to give technical accuracy, the surgical navigation system must have a planning interface for defining exactly where each pedicle screw is intended to be placed. In our studies, we either measured technical accuracy as a 2D distance (from an in-line coronal view of the pedicle screw trajectory) or as simple distances in the axial and sagittal plane (1, 3). We also typically included the angular deviations in axial and sagittal views.

3.5 VIRTUAL GERTZBEIN GRADING

In studies where the placement of pedicle screws was not possible and only Jamshidi needles or K-wires were placed, a simulation of the Gertzbein grading scale was used (3). In these studies, the pedicle device width was extrapolated to common pedicle screw diameters, as has previously been published (62). The minimal distance between the pedicle device and pedicle wall was measured for each pedicle (in an in-line coronal view along the pedicle device axis). Then, screws of either four, six, or seven mm diameter were simulated, and the resulting distance from the pedicle wall was judged according to the Gertzbein grading scale: grade 0 (screw within pedicle), grade 1 (breach < 2 mm), grade 2 (breach 2 – <4 mm), and grade 3 (breach ≥ 4 mm). The choice of screw diameter to be simulated for each pedicle was defined as the largest diameter possible without exceeding the thickness of the actual pedicle. Where screw diameters were larger than the pedicle width, a one-step-smaller screw diameter was simulated.

3.6 DIFFUSE REFLECTANCE SPECTROSCOPY (DRS)

In **Paper V**, tissue was probed using an integrated pedicle screw and screwdriver (see Figure 9) equipped with two optical fibers at the tip of the screw (6). The tool consisted of an inner stylet containing the optical fibers, leading to the tip of the screw, that allowed for turning the tool without twisting the optical fibers. An in-depth description of the tool setup has been published previously (111). One fiber was connected to a broad-spectrum halogen light source to transmit light into the tissue, while the other was used to receive reflected light. Typical pedicle screw breaches were planned and carried out using augmented reality surgical navigation. DRS measurements were done at regular intervals or at specific places where either the surgical navigation system or the surgeon indicated a change from cancellous to cortical bone or external tissues, or the DRS indicated a change. Each DRS collection position was verified either by cone-beam computed tomography or by inference where the position was known to be somewhere between two verified points, and only one tissue type was present between them.

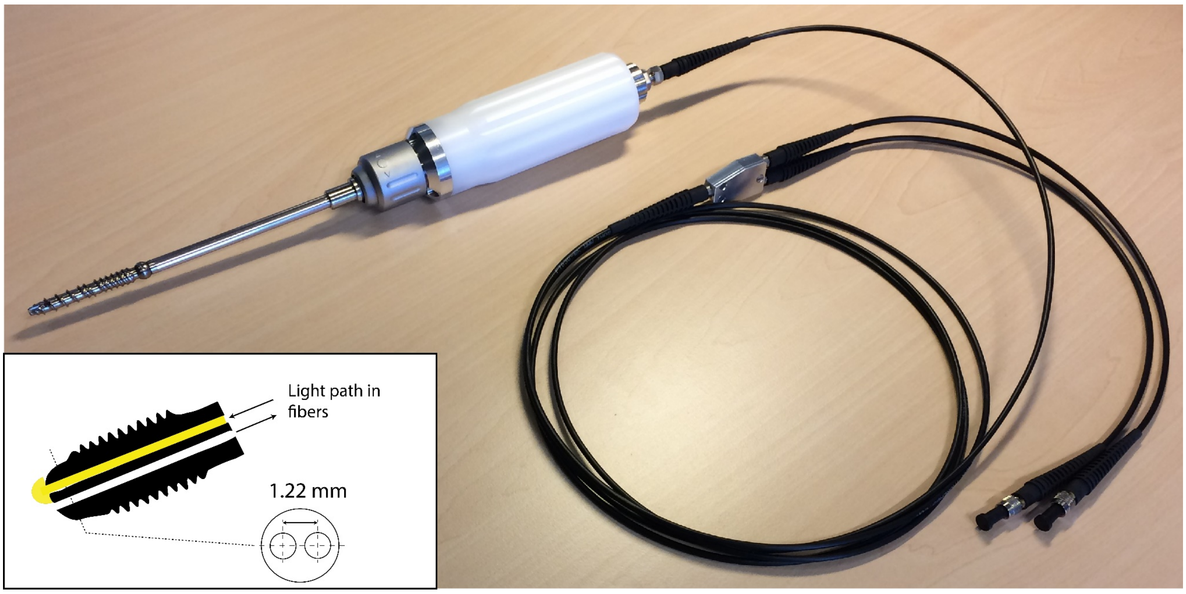

Figure 9. DRS probe used in Paper V. Inside the probe, a freely rotating styled carries optical fiber to the tip of the pedicle screw. Note that the pedicle screw part is integrated with the tool, unlike a true pedicle screw. Figure reproduced from Burström et al (6). (© 2019 Optical Society of America. Users may use, reuse, and build upon the article, or use the article for text or data mining, so long as such uses are for non-commercial purposes and appropriate attribution is maintained. All other rights are reserved.)

DRS measurements acquired from the pedicle screw insertions were analyzed in the wavelength range of 400 to 1600 nm. A fitting algorithm was used in which the measured spectra could be translated into meaningful physiological or chemical parameters, as previously described (100, 106, 121).

3.7 SUPPORT VECTOR MACHINES

In **Paper V**, the performance of DRS in detecting an impending breach using multiple tissue constituents and physical parameters was evaluated (6). To this end, a support vector machine (SVM) classification methodology was used (122). Before training the SVMs, all features were scaled to a mean of 0 and a standard deviation of 1. For training the SVMs, RStudio (RStudio Team. RStudio: Integrated Development for R. RStudio, Inc., Boston) and the e1071 package (Probability Theory Group, 2019), based on LIBSVM (123), was used with a radial kernel and standard parameters (cost: 1, and gamma: 1/no. of data dimensions).

The method was employed in two ways. First, a 1:2 ratio split was used to train a model on 66% of the data. The remaining 33% was used as validation data to calculate accuracy, sensitivity, and specificity for the model based on the confusion matrix of the validation data. Second, a leave-one-specimen-out cross-validation approach was used where the classification models were trained on all but one cadaver, and the validation was performed on the remaining cadaver. This was done in order to show how the method work on truly independent data. Validation was only performed on cadavers with more than five tissue readings in both cancellous and cortical bone to ensure enough validation data. This approach was repeated until all included cadavers had been left out once, with the confusion matrices being added.

4 RESULTS & DISCUSSION

Pedicle screw placement during spine surgery is generally safe and provides a reliable way of fusing multiple vertebral levels. However, there are two potential advantages in using technological aids instead of freehand (FH) surgery for pedicle screw placement. First, with reliable aiding technologies, extremely complex or otherwise risky surgery can be performed under more controlled circumstances. This could either enable surgery that was previously deemed too risky compared to the potential benefits or reduce risks associated with essential but high-risk surgery. Secondly, with unobtrusive and easy-to-use aiding technologies, there is a possibility to use the technology as the standard of care in each surgical case when performed as a way to prevent rare but potentially crippling complications in regular spine surgical cases. To this end, wrong-site surgery (vertebral level or side) and severely misplaced pedicle screws could be minimized in everyday spine surgery.

In this thesis, technological solutions fitting both of these use cases have been studied. In our experimental setups, the systems have not necessarily been optimized for either purpose. Due to the technological complexity and the necessary integrated solutions to different aspects of navigation, each part of a technological solution cannot vary while keeping the others constant. For example, it has not been possible to vary the patient-tracking technology (regular cameras and skin fiducials compared to infra-red cameras and DRFs) while keeping the rest of the system constant (i.e., the same AR interface and intraoperative imaging technology). Instead, we have aimed to study what technology is available (**Paper II**) and to test additional technologies supplementing the basic navigation setup iteratively, in the form of instrument tracking (**Paper III**) and robotic aid (**Paper IV**).

4.1 AUGMENTED REALITY SURGICAL NAVIGATION PROVIDES A HIGH ACCURACY

In our clinical cohort study (**Paper II**), the use of AR navigation provided an accuracy of 94.1% for pedicle screw placement (for full data, see Figure 10)(4). This reflects previously published accuracy rates for navigated systems, with accuracies ranging from 90.2% to 98.6% (124-129). The main point of our study was to investigate whether AR navigation is comparable in accuracy to other navigation systems, not necessarily if it is superior. AR navigation instead of traditional navigation, which is usually referred to as VR in the field, could have the benefit of improving usability by displaying navigational information directly in the surgical view. This could minimize the impact on workflow, enabling the surgeon to focus on a single place in the surgical field instead of switching viewpoints between the surgical area and a separate VR display. However, this specific hypothesis was not part of our research and remains for future studies to investigate.

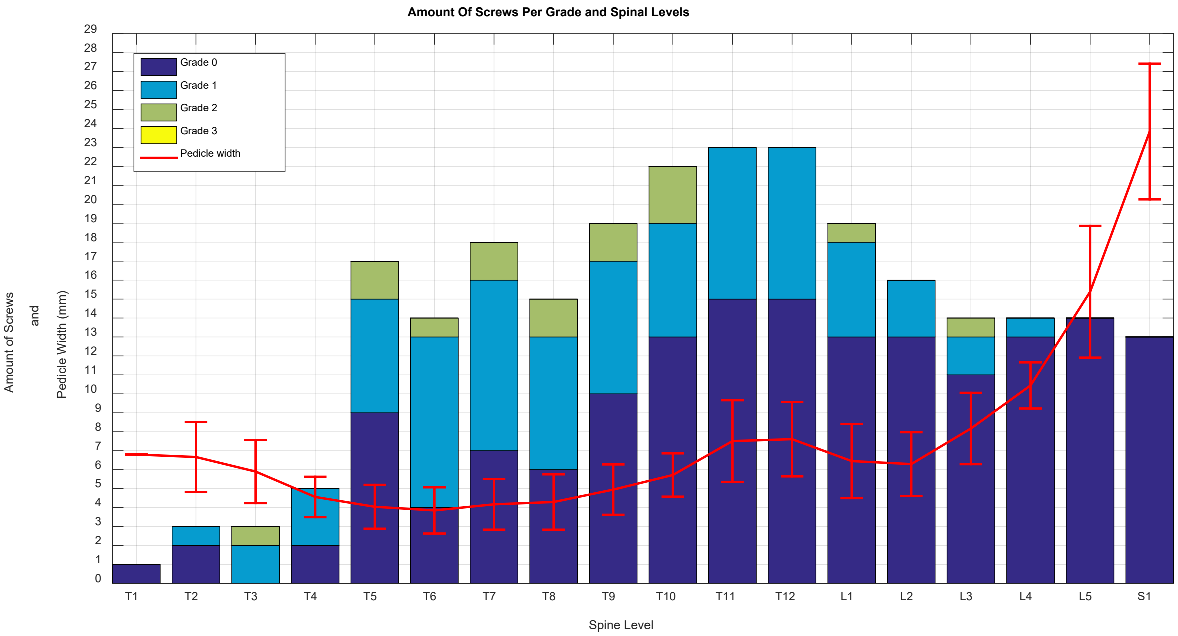

Figure 10. Distribution of pedicle screws Histogram depicting number of screws per level (height of columns) and by Gertzbein grading (column colors). Red line indicates corresponding mean pedicle widths per level, and red bars indicate standard deviation. Republished with permission from Elmi-Terander & Burström et al (4).

It is important to highlight that the variation in accuracy between studies is not only associated with differences in the navigation technology used or the experience of surgeons. Previous studies indicate narrow pedicles are an important risk factor for pedicle breach (130, 131). The narrowest pedicles are in the mid-thoracic (T5-T8) levels with an average width of 4 mm (130, 132). Subsequently, the share of mid-thoracic pedicles in a study cohort would have an impact on the accuracy reported in the study, and our data was in line with this finding, as seen in Figure 10. During our work, we found that there was indeed a correlation (-0.90, $p<0.05$) between the percentage of thoracic screws in studies (ranging from 8.2% to 73.9%) and the achieved accuracy (90.2% to 98.6%)(124-129). The share of thoracic screws in our study was 64.4%, representing the upper part of studies reporting the share of thoracic pedicles and demonstrating that our results are not simply due to favorable patient selection.

In a follow-up study, the same patient cohort was compared to a historical cohort, operated on by the same surgeon. We could show a statistically significant improvement in accuracy for AR-navigated surgery compared to FH surgery (133). This further corroborates the conclusions of Paper II.

4.2 ACCURACY AND OPERATING ROOM TIME CAN BE IMPROVED WITH MACHINE LEARNING METHODS

The use of surgical navigation may impair valuable operating room (OR) time if the system is not optimized for an efficient workflow. When intraoperative 3D imaging is used, a certain amount of time is typically spent on planning navigation trajectories in the OR (54). However, a perceived increase in OR time is one of the main concerns cited by surgeons who refrain from adopting the technology (13).

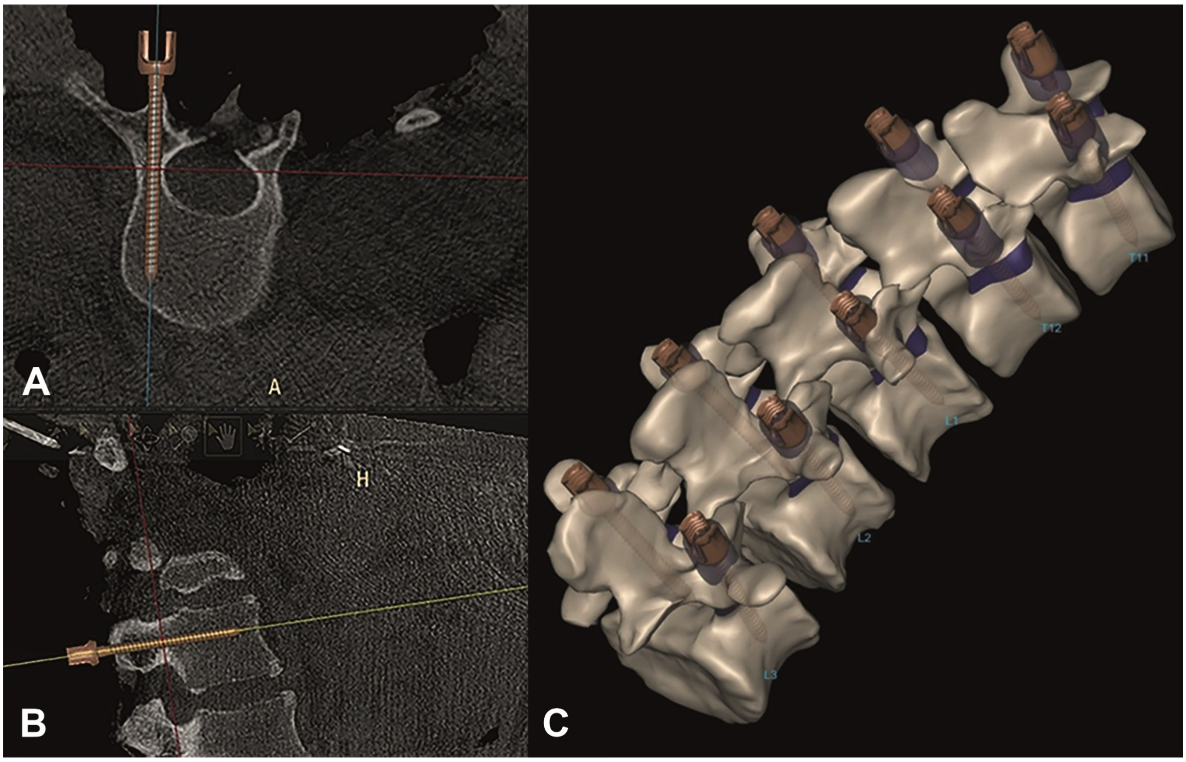

Figure 11. Interface depicting automatic screw suggestion. In A and B, axial and sagittal CBCT view. In C, the automatic segmentation (3D representation) of the scanned vertebrae. Note that in clinical use, only an entry point is suggested, while length and trajectory needs to be actively done by surgeon. Republished with permission from publisher, original work by Burström et al (2).

In **Paper I**, a machine-learning algorithm was developed for the identification of vertebrae, vertebral components including pedicles, and suggestion of a pedicle screw trajectory automatically based on the intraoperative 3D imaging (Figure 11). This algorithm was then validated on 20 patient radiographs for a total of 316 pedicles and suggested pedicle screws. A clinically adequate pedicle segmentation was attained in 86.1% of pedicles (Figure 12). In a post-hoc analysis, we identified that 75% of failures occurred in patients where (1) the Cobb angle was >75 degrees, (2) previous surgery had severely changed the anatomy of the vertebrae, or (3) severely degenerated vertebrae were present. If the algorithm was only used outside of these suggested exclusion criteria, our data suggested a clinical accuracy of 95.4%. This accuracy, however, will need to be validated in a new patient set to confirm our post-hoc analysis.

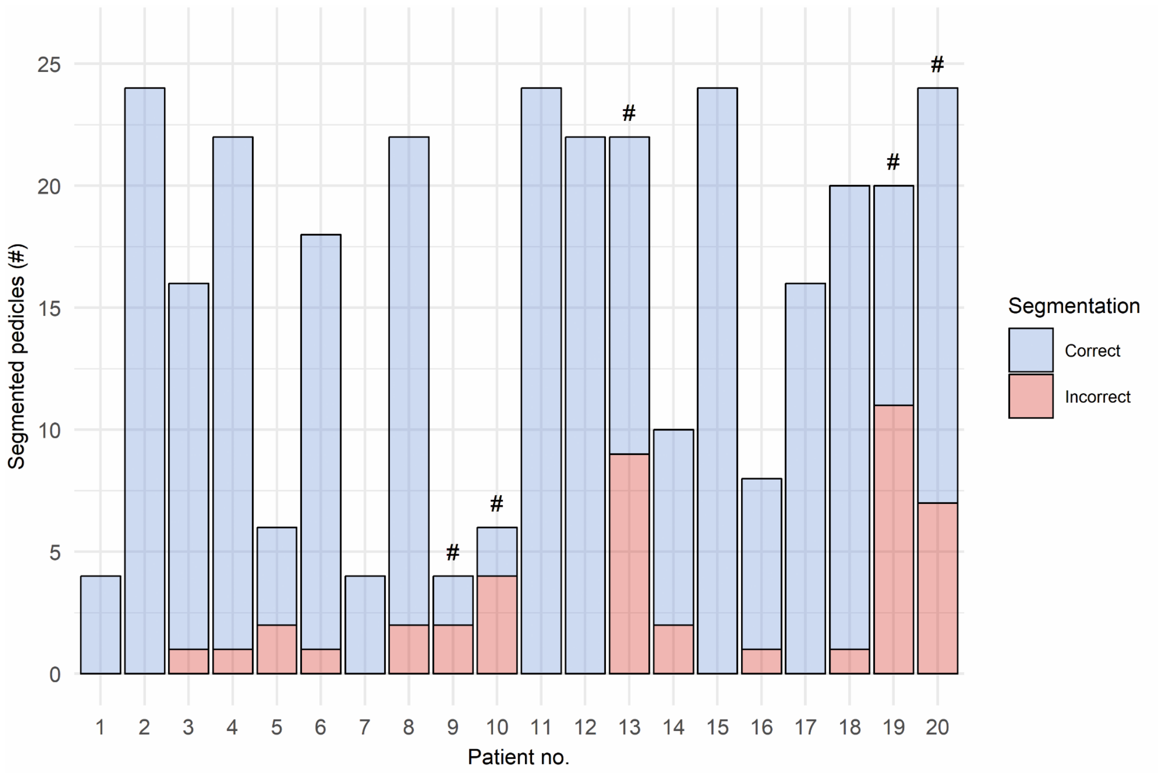

Figure 12. Pedicle segmentations per patient. Distribution of correctly (blue) or incorrectly (red) segmented pedicles per patient. Patients highlighted with pound sign (#) had one or more exclusion criteria. Republished with permission from publisher, original work by Burström et al (2).

An important aspect of bringing our results into a clinical routine is that the failure of the algorithm must not translate into clinical mistakes. Therefore, these and similar machine-learning solutions to workflow and OR time-related problems need to be designed in a manner that maintains patient safety. In this case, the interface can be designed so that the suggested pedicle screw must be actively confirmed by clicking it or dragging it out to a preferred length. This prevents surgeons from inattentive validation of misplaced screw suggestions, as they must interact with the plan in question for each screw. Naturally, this does take a certain amount of time, but it is negligible compared to making the plan from the start.

4.3 NAVIGATED INSTRUMENTS IMPROVE AUGMENTED REALITY NAVIGATION ACCURACY

In **Paper III**, the effect of adding instrument tracking during surgery to the same surgical navigation system as used in **Paper II** was examined. As a necessary part of this addition, the user interface was also somewhat altered compared to what was used in Paper II to accommodate visualization on axial and sagittal views for said instruments (Figure 13). This was called a mixed AR and VR interface. Seventy-eight insertions of K-wires into the pedicles of pig cadavers were performed. We found that the technical accuracy at bone entry was 1.7 ± 1.0 mm. Each K-wire thickness was then extrapolated to typical pedicle screw diameters for each postoperative scan, noting if these virtual pedicle screws would have resulted in a breach and assigning a Gertzbein grading. Using this virtual Gertzbein grading, an accuracy of 97.4 to

100% was demonstrated for pedicle screw diameters of up to 7 to 4 mm, respectively. The effect of using different surgical methods was also evaluated by comparing the accuracy of either drilling or hammering in the pedicle devices. There were no statistical differences between the two methods (p = 0.8 at tip, p = 0.88 at bone entry).

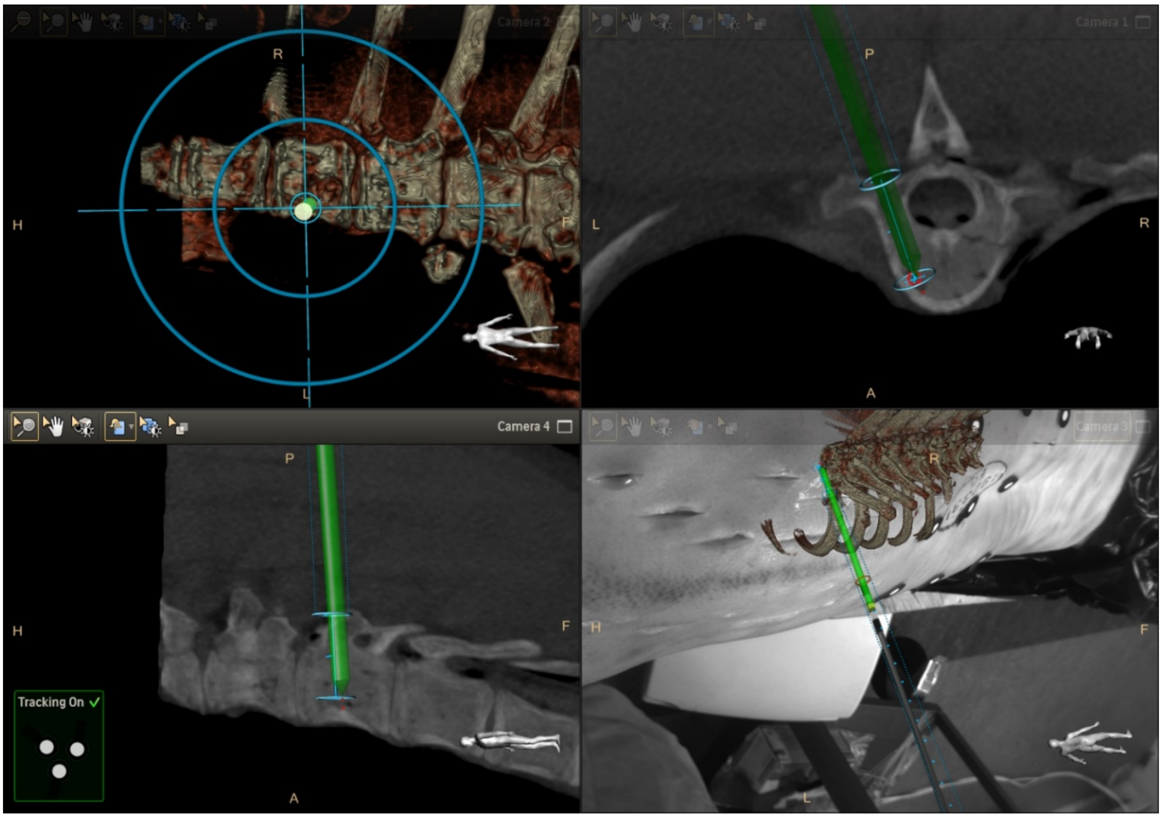

Figure 13. AR and VR interface. Top left shows VR view along trajectory. Top right shows VR axial, and bottom left shows VR sagittal view. Bottom right shows AR view of surgical area. Green 'stick' represents tracked Jamshidi needle. Republished with permission, original by Burström et al (3).

A direct comparison with the 94% accuracy in our previous patient cohort (**Paper II**) entails several uncertainties (4). When using instrument tracking, we performed all experiments on pig cadavers instead of patients, and all pedicle screw diameters were extrapolated from K-wires. However, previous studies on human cadavers, using the same navigation system and outcome measurements as in **Paper II**, resulted in a technical accuracy of 2.2 ± 1.3 mm. This indicates that the addition of instrument navigation likely leads to increased accuracy. However, further studies will be needed to confirm this finding, as the study was designed to serve as a first proof-of-concept for the technology.

4.4 ROBOT SURGERY FURTHER REDUCES NAVIGATION ERRORS

In **Paper IV**, a robotic arm was added to the system used in **Paper III**. In all other aspects, the navigation system was the same. We placed 113 Jamshidi needles in the pedicles of four human cadavers. The mean compound (2D) technical accuracy at the bone entry point was 0.94 ± 0.59 mm (see Figure 14). When extrapolating the Jamshidi needle diameter to common pedicle screw diameters, a clinical accuracy of 100% was found irrespective of the maximum screw diameter assumed.

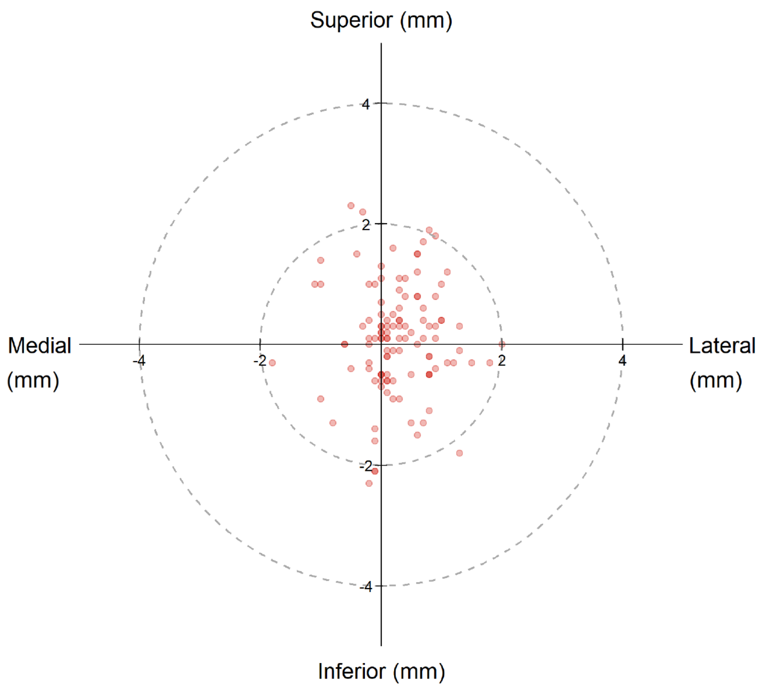

Figure 14. Technical accuracy of robot surgery. Red dots represents position of each pedicle device relative to the intended target (position x=0, y=0). Republished with permission, original work by Burström et al (1).

The methods in **Paper IV** were similar to those used in **Paper III** except for the robot arm used, and the surgeries were performed on human cadavers instead of pigs. The difference between placing pedicle devices in pig cadavers and human cadavers depends to a large extent on the size of the pig and, hence, the size of the pedicles. The mean size of the pedicles in **Paper IV** was 7.3 ± 2.3 mm, while the mean pedicle width in **Paper III** was 7.1 ± 1.2 mm; in terms of pedicle devices, these values are reasonably similar. Other potential confounders in comparing the two studies could be the entry point anatomy, which, if on a slope, can increase the tendency of skiving while entering, leading to decreased accuracy (86). Yet another potential confounder is the depth at which the entry point is located, which in pigs is somewhat deeper (with the potential for decreased accuracy). Bearing these differences in mind, the data suggested that the addition of a robotic arm leads to increased accuracy. Most notably, we saw a reduction of large outliers, indicating that the most misplaced screws—and possibly the most damaging ones—could be prevented.

Another aspect in the addition of a robot arm is the impact on workflow and OR time. The system was a prototype not optimized for workflow; thus, it did not lend itself to study in this regard. However, data on the mean navigation time was 96 ± 37seconds from skin incision to placement of a Jamshidi needle. In **Paper III**, the comparable mean time was 195 ± 93 seconds. In robot studies reporting comparable surgical times, the mean time per pedicle cannulation was 202 to 257 seconds (134, 135). The above-mentioned times do not reflect true OR times, though, as large portions of the surgical work are not included and should only be used for direct comparisons of other, similar cadaveric studies. In addition, the setup times were not included, which will be a crucial part of the clinical evaluation of such a system for determining the impact of its workflow and OR times.

4.5 DRS SHOWS PROMISE FOR DETECTING IMPENDING PEDICLE SCREW BREACH

In **Paper V**, we demonstrated that a diffuse reflectance spectroscopy (DRS) probe built into the tip of a pedicle screw could detect the cortical border of the vertebral bone. We showed that this worked in several different situations and breach directions (anterior, lateral, medial, and inferior). Based on lipid and collagen content, there was a significant difference between cancellous and cortical bone and a clear transition zone between them. An example of data obtained from an anterior breach is presented in Figure 15. Several previously validated machine-learning algorithms were used to extract predicted tissue constituents (e.g., lipid, water, and blood content) and physical properties (e.g., scattering at 800 nm, Mie scattering) in the vertebrae. To test the usefulness, we applied a support vector machine (SVM) that was trained on all cadavers but one and then tested it on the last one, using multiple crossovers until all cadaver data had been left out once (i.e., leave-one-out methodology, LOO). This resulted in a sensitivity of 98.3% (94.3%–100%) and a specificity of 97.7% (91.0%–100%) for detecting the cortical border before resulting in a breach of the cortical wall.

The technology and the research regarding its usefulness in spine surgery are still in their early stages. The current study was the first study imitating a true surgical setup, including a custom-built DRS probe that functioned as a pedicle screw, to collect data as close to surgical reality as possible. Consequently, all predictions and accuracy tests were performed on data from the same setup. This has the inherent problem of only validating the exact settings of our experiment and not necessarily a true surgical scenario. To mitigate similar effects, LOO methodology was used when testing sensitivity and specificity: each cadaver was treated separately and treated as a test subject that was never included in the original data used to train our models. However, this method cannot exclude specific influences on the data coming from the experimental setup, which would be slightly different during real surgery. The most important known difference is that all experiments in Paper V were performed on human cadavers; thus, no blood perfusion was present. Since hemoglobin and oxyhemoglobin are two strong chromophores that influence the DRS data, they present a potential problem when translating the research from cadaver models to live subjects. Therefore, a follow-up study was done on a live pig, suggesting that the presence of perfusion does not significantly alter our conclusions (136).

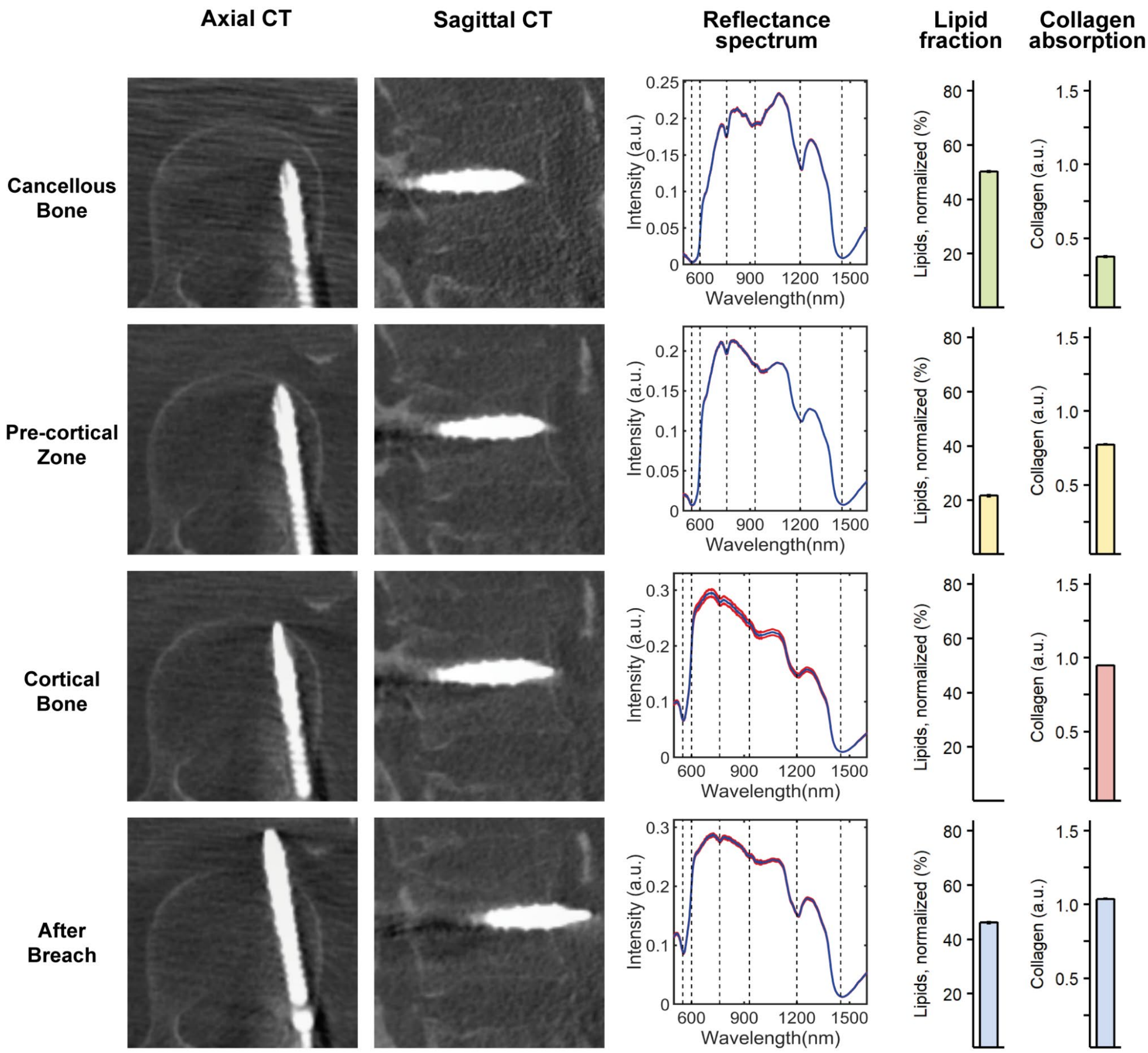

Figure 15. Example of DRS readings during pedicle screw breach. The first and second columns show axial and sagittal computed tomography of each position, respectively. The third column shows acquired spectra at each position in red and the fitted spectrum in blue. The fourth and fifth columns show the measured lipid and collagen fractions, respectively. Figure republished with permission, originally work by Burström et al (6). (© 2019 Optical Society of America. Users may use, reuse, and build upon the article, or use the article for text or data mining, so long as such uses are for non-commercial purposes and appropriate attribution is maintained. All other rights are reserved.)

4.6 FUTURE PERSPECTIVES

Surgical safety and accuracy result from a combination of factors. The most important one is the understanding of surgical anatomy. A screw placed perfectly, according to superficial anatomical landmarks, can still be placed poorly if the underlying anatomy was different than expected, or if the original plan was flawed. Computer-assisted navigation can present the relevant underlying anatomy into the direct view of the surgeon to improve real-time understanding of surgical anatomy and trajectories. This presents new possibilities for spine surgery, as well as potential problems to note. Image fusion and segmentation algorithms need to provide a seamless combination of CT and MRI imaging data without errors. Software solutions must be tailored or customizable to the intended use so that they assist in creating the best surgical plans rather than force the surgeon to adjust the surgical technique to compensate for technological flaws.

In a seemingly never-ending effort to reduce surgical errors, the introduction of robots has been a natural step, as demonstrated by the constituent papers of this thesis. However, neither the surgeon nor the navigational system can see inside the body, and no amount of preoperative planning or imaging can solve this inherent problem. While tracking reference markers, the navigational system does not provide true feedback on where the tip of an instrument is inside the body. Thus, bending of instruments when pushed against dense bone is only felt by the surgeon and not seen by the navigational system. Similarly, small movements of the spine may remain undetected. These problems are compounded if control of the surgical instruments is relinquished to a surgical robot. Supplementing a surgical or robotized navigation system with sensing equipment has the potential to address these issues. An all-integrated system of the technologies discussed in this paper is not hard to imagine. In the following paragraphs, the different aspects and components of such a solution are discussed.

Precise tracking using cameras and machine learning

Accurate, uninterrupted tracking of the patient is essential for navigated surgery. The most common tracking solution used currently is the DRF, which is often designed as a metal star or cross with reflective spheres at the points. The three-dimensional relation between the spheres is recognized by the navigational system, and their position in space is fixed in relation to the patient and the imaging data during patient registration. However, the metal star must be positioned in the vicinity of the surgical field; if it is dislodged, accuracy may be lost. Alternatives, such as the adhesive markers used in the constituent papers in this thesis, reduce the problems associated with a bulky DRF but still add to the complexity of performing a navigated surgery. Furthermore, they do not accurately represent vertebral movements at highly mobile levels such as the upper cervical area since they track the overlying skin and not the actual vertebrae. Future solutions could implement marker-free alternatives where the cameras of the navigational system see the patient and continuously track both the patient and the instruments within the surgical field. In this context, AR technology is well suited since it can provide visual feedback on the accuracy of the alignment of real-world and virtual objects.

For example, using machine-learning methods optimized for the interpretation and tracking of visual objects, the surface-level anatomy could be tracked using only cameras and software. In a newly published article our group investigated such a method, in which we applied a computer vision framework to process spine images (68). Using common algorithms in image processing, spine features could be detected and used for 3D triangulation, reaching an error of the matched features below 0.5 mm. Spine feature tracking offers an extension and an improvement of current tracking systems, in that it identifies the specific targeted anatomy directly and without invasive markers. By tracking features directly related to each vertebra in the surgical field has the potential to be more accurate than DRFs, which only provide tracking of a single vertebra, or patient-tracking techniques with indirect relationships to the vertebrae (68, 137, 138).

Although spine feature detection offers high accuracy, the technology can only be employed in open surgical cases where spine features are visible. However, similar algorithms could be used for marker-less skin feature detection to aid in MISS cases. In another recent study, we applied these methods in combination with hyperspectral imaging of the skin, and we showed promising results while obtaining a TRE below 0.5 mm (69). This may also be implemented on continuous ultrasonographic images if such a surgical setup was employed, allowing mobile upper cervical vertebrae to be continuously tracked even during MISS cases.

Updating the surgical situation in the navigation software

Perhaps the easiest way to update the preoperative imaging used for navigation with these intraoperative changes involves the use of 2D fluoroscopy to obtain at least two different image views, followed by using these views to adjust or renew the co-registration. The strategy, already used for the first generations of the Mazor robot, has been further developed by several companies (139, 140).

A CT or CBCT update provides the possibility of a 3D re-alignment, offering higher accuracy since the updated images can align better with the previously planned paths and surgical course. As a prerequisite for this functionality, the navigation plan from the start of the procedure can be fused with new intraoperative images without re-planning or manual realignment.

The most advanced future form would employ visual updates using cameras and machine-learning algorithms, similar to the case discussed in the previous paragraphs. Instead of only tracking surface anatomy to compensate for shifts or rotations of vertebrae, a future advanced algorithm could indicate visible surgical changes to the anatomy. Such changes could involve a laminectomy performed during surgery or updated tumor outlines while the tumor is removed to represent the surgical situation optimally in real-time. However, this option is still relegated to the future, as suitable algorithms for 3D reconstruction are still lacking, and the computational power would most likely exceed the limits of today’s AR systems.

4.7 ETHICAL CONSIDERATIONS

This thesis includes scientific work performed on dead animal models, human cadavers, and live patients. Thus, multiple ethical considerations have been made. Generally, all ethical considerations are motivated by the fact that current surgical approaches lead to widely reported complications for patients, including vascular and neural injuries and the need for revision surgeries. Thus, new technologies with the potential to remedy these issues are of high value to patients to increase safety.

Regarding the dead animal models, this work (**Paper III**) concerned completely new and untested features of the ARSN system. Thus, it requires accurate tissue models of vertebrae and pedicles both anatomically and structurally to reflect the surgical use of the system. We had the choice to use a animal cadaver model or a human cadaver model. The former was considered to have the fewest negative ethical implications.

Regarding the use of diseased humans in cadaver experiments, all work was done in the USA (Cincinnati, OH). The studies (**Papers I, IV, and V**) were conducted in compliance with ethical guidelines for human cadaver studies in the USA. Since none of the studies involved the collection of identifiable private information, they were exempt from the need for specific study ethical approval under United States legislation number 45 CFR § 46.102. All work on cadavers strictly adhered to all rules and regulations of the Health Insurance Portability and Accountability Act (HIPAA). Informed consent for donation to scientific research had been signed before death by the donors or after death by relatives, according to the local guidelines approved by the University of Cincinnati College of Medicine (COM). COM allows donated human cadavers to be used for medical education, the advancement of medical science, and research for the development of medical products and techniques. This includes allowing donated human cadavers to be used by researchers at CCHMC and other institutions, including our research group. All work done on cadaver models involved more mature technologies than those using animal models. We conducted these experiments as a final confirmatory step before testing the technology on patients, considering it ethically motivated to maximize our understanding before testing it on live patients.

Lastly, the study involving human subjects (**Paper II**) was motivated by preclinical studies indicating that the technology seemed to provide superior surgical results compared to conventional surgical methods. Thus, after ethical approval and informed consent, we offered patients the choice of participating in testing the ARSN technology. All patient information was kept either on paper in locked boxes in the hospital or anonymized on the work laptops of participating co-authors working in the hospital.

5 CONCLUSIONS

Paper I demonstrated that a system for automatic vertebral segmentation and pedicle screw planning could provide clinically reliable suggestions in 86.1% of pedicles. By excluding patients with severe spinal deformities and previous surgeries, the result was 95.4%. This type of technology has the potential to support the surgeon in pedicle screw planning when using surgical navigation, thereby reducing surgical errors and saving valuable OR time.

Paper II showed that the use of augmented reality surgical navigation (ARSN) in a hybrid operating room resulted in 94.1% of placed screws being graded as Gertzbein grade 0 or 1, representing correctly placed screws.

Paper III demonstrated that the addition of instrument tracking to ARSN in a hybrid OR was feasible and facilitated navigation for the placement of pedicle devices, resulting in 97-100% of pedicle devices graded as accurate.

Paper IV showed that the addition of a robotic arm to the ARSN system was feasible and resulted in higher clinical and technical accuracy compared to non-robotic attempts while reporting a lower device placement time.

Paper V demonstrated that DRS technology reliably identified the area of transition from cancellous to cortical bone in typical breach scenarios. DRS technology in the tip of a surgical instrument has the potential to help the surgeon to avoid pedicle screw breach in spinal fixation surgery.

Future challenges in the field of computer-assisted surgery

Although studies on accuracy have shown the benefits of using surgical navigation in spine surgery, **the field still lacks high-quality studies on the clinical outcomes** of patients when using the technology. Perhaps the most important next step for the research field will be to perform randomized controlled studies studying the effects on patient outcomes such as mortality, revision surgery, and morbidity in the form of neural injuries, vascular injuries, and pain.

Even if potential benefits are shown, for surgical navigation, robotics, and sensing technologies to become part of clinical routine, there will be **a need for rigorous cost-benefit studies**. One of the major reasons cited for not using surgical navigation today is its costs (13).

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