Appendices Report

Development and Evaluation of an Integrated Medical Imaging Workstation for Diagnostic and Surgical Planning Support in Pancreatic Cancer

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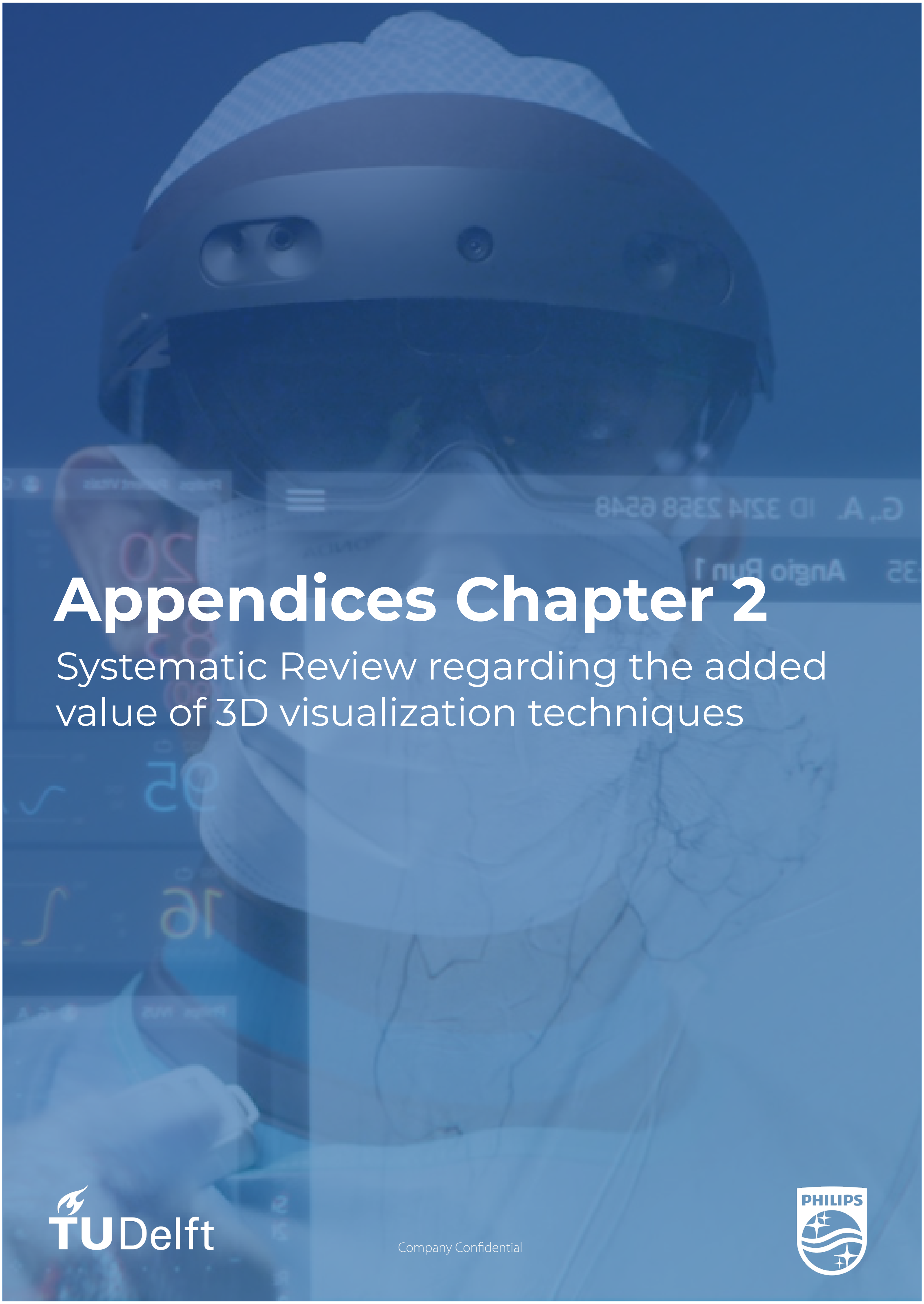

Appendices Chapter 2

Systematic Review regarding the added value of 3D visualization techniques

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The added value of 3D Visualization Techniques during the Preoperative Planning of Complex Oncological Resection Surgery: A Systematic Review.

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Abstract

Background Three-dimensional visualization techniques (3DVTs) including three-dimensional printing, virtual reality, mixed reality, and holographic displays, could potentially have an added value in planning complex surgical oncology procedures. The aim of this systematic review was to describe the added value of 3DVTs used during the preoperative planning of complex oncological resection surgery.

Methods A systematic literature review was performed by searching Pubmed, Embase, Web of Science, COCHRANE Library and Emcare from 2010 to October 14th, 2020. The literature search identified 908 articles, of which 20 articles were found eligible for the qualitative analysis. Data regarding study and technology characteristics and outcome measures (compared intra- and postoperative outcomes, questionnaires, and performance assessments) were extracted from the included studies.

Results Five studies reported intra- and postoperative outcomes regarding the operation time, estimated blood loss, clamp time, resection margins, hospital stay, complications and other procedural relevant outcomes. Eleven studies conducted questionnaires regarding the utility, experience, usefulness, anatomical understanding, or the surgical strategy used in the preoperative planning. Eight studies assessed the performance of surgeons regarding their anatomical understanding, resection time, surgical strategy, and planning time.

Conclusion The application of 3DVTs could reduce the operating time and estimated blood loss in complex surgical procedures. 3DVTs enable the surgeons with a better spatial anatomical that could lead to changed surgical strategies. In addition, surgeons are more confident choosing and performing surgical strategies. Both physical printed and digital stereoscopic models enhance surgeons with new pre- and intraoperative interaction possibilities. Further technological development needs to be done to eventually facilitate wide clinical implementation of 3DVTs.

Keywords Three-dimensional; virtual reality; mixed reality; three-dimensional printing; holographic display; pre-operative planning; complex surgical oncology.

List of abbreviations and acronyms

3D = Three-Dimensional
3D-on-2D = Three-Dimensional Reconstruction
3DP = Three-Dimensional Printing
3DVTs = Three-Dimensional Visualization Techniques
CT = Computed Tomography
HD = Holographic Display
MR = Mixed Reality
MRI = Magnetic Resonance Imaging
Non-3D = Non-Three-Dimensional
PICOS = Participants, Interventions, Comparisons, Outcomes and Study design
VR = Virtual Reality

Introduction

In surgical oncology, surgeons are primarily focused on the resection of the abnormalities in patients, especially cancerous tumors (1, 2). Main technical difficulties in performing these complex procedures successfully are the patient-specific anatomical variation and the assessment of the tumor interaction with other anatomical structures and especially the relevant vasculature (3). Therefore, careful examination of preoperative imaging data aids the surgeon to anticipate the irregular and unpredictable spatial conformation of the patient-specific anatomy and pathology (3).

In current practice, surgeons base their decisions based on the information given by conventional medical imaging scans created with imaging modalities such as computed tomography (CT) or magnetic resonance imaging (MRI). However, surgeons need to convert the information provided on the two-dimensional imaging slices into their own mentally constructed 3D representation of the anatomy. This creates a subjective understanding of the patient anatomy and is not easily shared among the involved clinical personnel (4, 5). Advancements in image processing techniques have made it possible to translate cross-sectional 2D medical imaging into three-dimensional (3D) reconstructions. These technological advances have certainly improved the preoperative planning and understanding of the patient-specific anatomy (6). Nevertheless, these 3D reconstructions are usually investigated on 2D displays that come with limitations regarding the real depth perception of the important structures (5).

Over the past ten years, 3D visualization techniques (3DVTs) like 3D-printing (3DP), virtual reality (VR), mixed reality (MR) and holographic displays (HD), shown in Figure 1 have drastically improved. Figure 1 illustrates the technology interaction of the abovementioned 3DVTs in context of a pancreatic cancer case. With 3DP, physical models of the human organs and their individual differences can be accurately printed using a wide variety of printing techniques (7). In VR, surgeons can interact with the virtual patient models in an interactive computer-generated 3D environment (8). MR can translate these virtual patient models into holographic reconstructions and superimpose these as on the physical world (9). Head-mounted displays (HMDs), also shown in Figure 1, are commonly used in VR and MR allowing a realistic and immersive experience. Finally, the reconstructed 3D models could also be displayed on HDs where no additional hardware is needed for a full 3D experience.

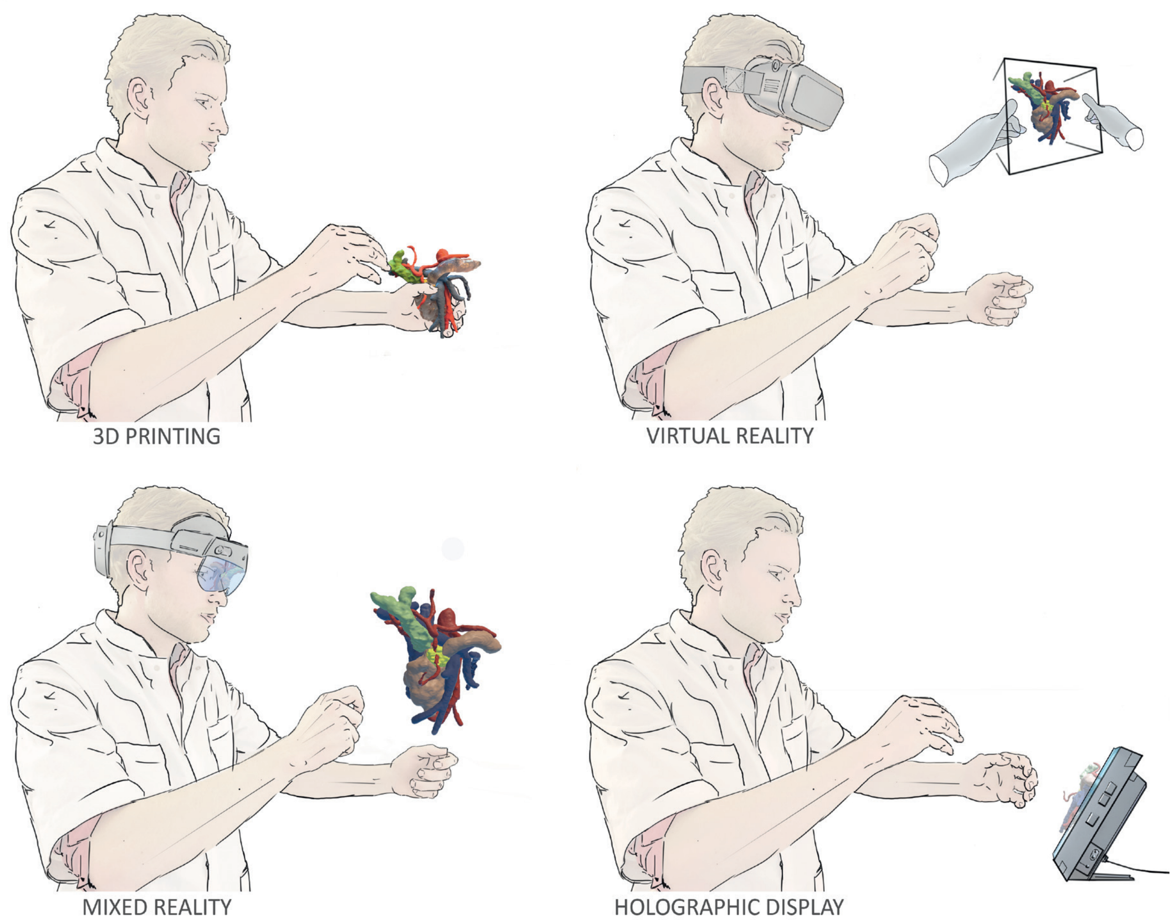

Figure 2.1. Drawings of the technology interaction of the different 3D visualization techniques (3D printing, virtual reality, mixed reality, and the holographic display) with an example 3D reconstructed pancreas cancer patient model. The pancreas cancer patient model has been obtained from a user-study within Eindhoven MedTech Innovation Centre (e/MTIC) oncology collaboration (Philips, Eindhoven University of Technology and Catherina Hospital Eindhoven). Illustrations are made by C.H. Broekmeulen and D.W.M. Rasenberg.

These 3DVTs, which are emerging in the field of medicine, could potentially be of great value for the surgeon in planning their complex tumor resection procedures. By studying the 3D rendered patient models with stereoscopic and immersive display and interaction technologies, the surgeon would be able to easily identify the malignant abnormalities and its interaction with essential structures. Ultimately, this could improve the clinical outcomes of complex oncological resection surgery.
Various applications of immersive and stereoscopic 3D techniques in subspecialties of cancer surgery have been described in the literature. For example, Checcucci et al (2020) assessed for example in a systematic review the preoperative and intraoperative impact of 3DP and virtual imaging for robotic nephron-sparing surgery (1). Furthermore, Quero et al (2019) provided an overview of VR-guided and AR-guided hepatobiliary oncologic surgery and its effects on the decision-making quality in the preoperative and intraoperative phase (8). However, to the best of our knowledge no article has systematically reviewed the available literature on these techniques applied during the preoperative planning in complex surgical oncology. Therefore, the objective of this systematic review is to describe the added value of 3DVTs used during the preoperative planning of complex oncological resection surgery.

Methods

A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement (10).

Data sources and search strategy

Five databases (Pubmed, Embase, Web of Science, COCHRANE Library and Emcare) were searched from the start of 2010 up to October 14th, 2020 to identify relevant articles. The usage of 3DVTs in medicine have drastically increased over the past ten years. Mainly due to technological advancements (e.g., image processing techniques, resolution, and accuracy) and the development of more affordable devices (11). Therefore, it was considered irrelevant to compare 3DVTs applications from before 2010 to currently available 3DVTs. A literature search was set up in collaboration with a clinical librarian. The following search terms to search all databases were used collectively to generate a relevant search strategy: three-dimensional visualization; augmented reality, mixed reality, virtual reality, 3D printing and holography; surgical oncology; diagnostic workup, treatment selection or planning. The exact search terms are provided Appendix 2.1.

Eligibility criteria

Eligibility criteria (Table 1) were defined before starting the screening and assessment of the literature. These eligibility criteria report characteristics which an article must contain in order to be included. The study characteristics are defined according to the PICOS components (Participants, Intervention, Comparator, Outcomes, Study design) described in the PRISMA statement (10). No comparison group was required in this review. Nevertheless, two comparison groups were defined, namely groups that used three-dimensional reconstructions on 2D displays (3D-on-2D) and groups that only used the conventional imaging techniques (non-3D). This review only considered English and Dutch written articles.

Article selection

The first author (D.W.M. R.) screened titles and abstracts in random order for relevance according to the predefined eligibility criteria. Secondly, a full text screening for eligibility was conducted on the articles that passed the first screening. References of selected articles were cross-checked for potentially relevant studies that were not identified in the original search. The full text of these studies was screened for eligibility if considered potentially relevant.

Quality assessment of studies

The study quality of each included article was assessed using an adjusted National Heart, Lung and Blood Institute (NIH) quality assessment tool (Figure 2)(12).

Table 2.1. Eligibility criteria

Study characteristics	
Participants	Patients (humans) of all ages who are/were diagnosed with cancer and have undergone tumor resection surgery.
Intervention	Patients who were exposed to oncologic surgery where 3DVTs (3DP, VR, MR and HD) based on diagnostic medical imaging were used for preoperative planning of the surgical procedure.
Comparator	No comparison group required.
Outcomes	- Compared (3DVT vs 3D-on-2D and/or non-3D) intra- and postoperative outcomes (operation time, estimated blood loss, clamp time, resection margins, hospital stay, complications, other procedural relevant outcomes). - Questionnaires regarding the utility, experience, effectiveness, anatomical understanding, or surgical strategy. - Surgical performance assessments regarding anatomical understanding, resection times, surgical strategy, and planning times.
Study Design	Randomized control trials, clinical trials, (prospective and retrospective) observational studies were included.
	(Systematic) reviews, case reports and studies, letter to the editor, comments on an article and no abstract/full text articles were excluded.
Report characteristics	
Language	Only English and Dutch written articles were included.
Year	Only articles from 2010 and on were included.

Modified National Heart, Lung and Blood Institute (NIH) quality assessment tool
(Yes = 1 point / doubt = 0.5 point / no = 0 points)

Questions regarding quality:
1. Was the study question / objective clearly stated?
2. Was the study population clearly and fully described?
3. Was the sample size sufficiently large to provide confidence in the findings (patients and evaluators)?
4. Was the intervention clearly described?
5. Was the technology clearly described?
6. Was the application / use of the technology comparable across study participants?
7. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across study participants?
8. Were the results well-described?
9. Were statistical tests used well-described?

Total score (max. 9 points)
Low quality = 5 points or less
Intermediate quality = 6 - 7 points
High quality = 8-9 points

Figure 2.2. Quality Assessment

Articles that scored 5 points or less were considered low study quality, 6-7 of intermediate study quality and 8-9 of high study quality.

Data extraction

Study characteristics, technology characteristics primary outcomes from the included studies were extracted. No meta-analysis was conducted, since the outcomes of the included literature were qualitative and therefore pooling of data was not possible.

Results

Search strategy

In the search strategy, 908 articles were identified from five different databases. After excluding the duplicates and articles that did not meet the language and year restrictions, 489 articles remained. Eventually, 20 articles were found eligible for the qualitative analysis in this systematic review. The PRISMA flow chart, corresponding to the search results, is given in Figure 4.

Study quality

The quality of the included 20 articles was assessed according to the adjusted National Heart, Lung and Blood Institute (NIH) quality assessment tool (12) as presented in Figure 2. Five articles included in this systematic review were of 'low quality', eight articles of 'intermediate quality' and seven articles of 'high quality' (Appendix 2.2). Liu et al (2019) scored the highest and had a QA score of 9/9 and Shi et al (2014) scored the lowest and had a QA score of 3/9. Most studies had a relatively small sample size and therefore scored 1 point less.

Study characteristics

The characteristics of the 20 included articles were divided over two groups based on the type of technology used. The physical printed model group (n=11) comprises all the studies reporting about the application of 3DP during the preoperative planning in complex surgical oncology. The digital stereoscopic model group (n=9) comprises all the literature reporting about VR, MR and HD applications for the same purpose. The relevant study characteristics are provided in Appendix 2.2. One article, Wellens et al (2019), reported both on 3DP technology and MR technology. Therefore, this study was included in both groups.

The three main reported surgical procedures were partial and/or radical nephrectomy (kidney, n=13), brain cancer resection surgery for multiple kinds of brain tumors (n=3) and anatomical partial lobectomy (lung, n=2). The other reported procedures were about the application of 3DVTs on segmentectomy/hepatectomy (liver, n=1), pelvic lymph node dissection prostatectomy (n=1), splenectomy and pancreatectomy (n=1) and periarticular tumor resection surgery (n=1).

Technology characteristics

The main imaging modality, the software to reconstruct the 3D models and the visualized anatomical structures were considered as relevant technology characteristics for both the physical printed model group and digital stereoscopic model group (Appendix 2.3). All the studies based their 3D reconstructions on CT and/or MRI scans. Many included studies used contrast enhancements for a better visualization of the relevant vasculature. Some studies reported on CT angiography and positron emission tomography (PET). However, these techniques have not been used for the reconstructions of 3D models. The main imaging modality and the 3D reconstructions were used for the visualization of the tumor, the relevant arteries and veins close to or interfering with the tumor, the organ parenchyma (functional part of the organ), relevant nerves close to the tumor and other relevant structures such as the renal collecting system.

Software used to segment and/or reconstruct the 3D models from the medical imaging includes, but is not limited to, Mimics (Materialise, Leuven, Belgium) (7, 13-17), Meshmixer (Autodesk, Venice, CA, USA) (9, 14, 18), ITK-SNAP (University of Pennsylvania, Pennsylvania, USA) (9, 19), 3D Slicer (https://www.slicer.org/) (20) and Unity (Unity Technologies, San Francisco, CA, USA) (4, 5).

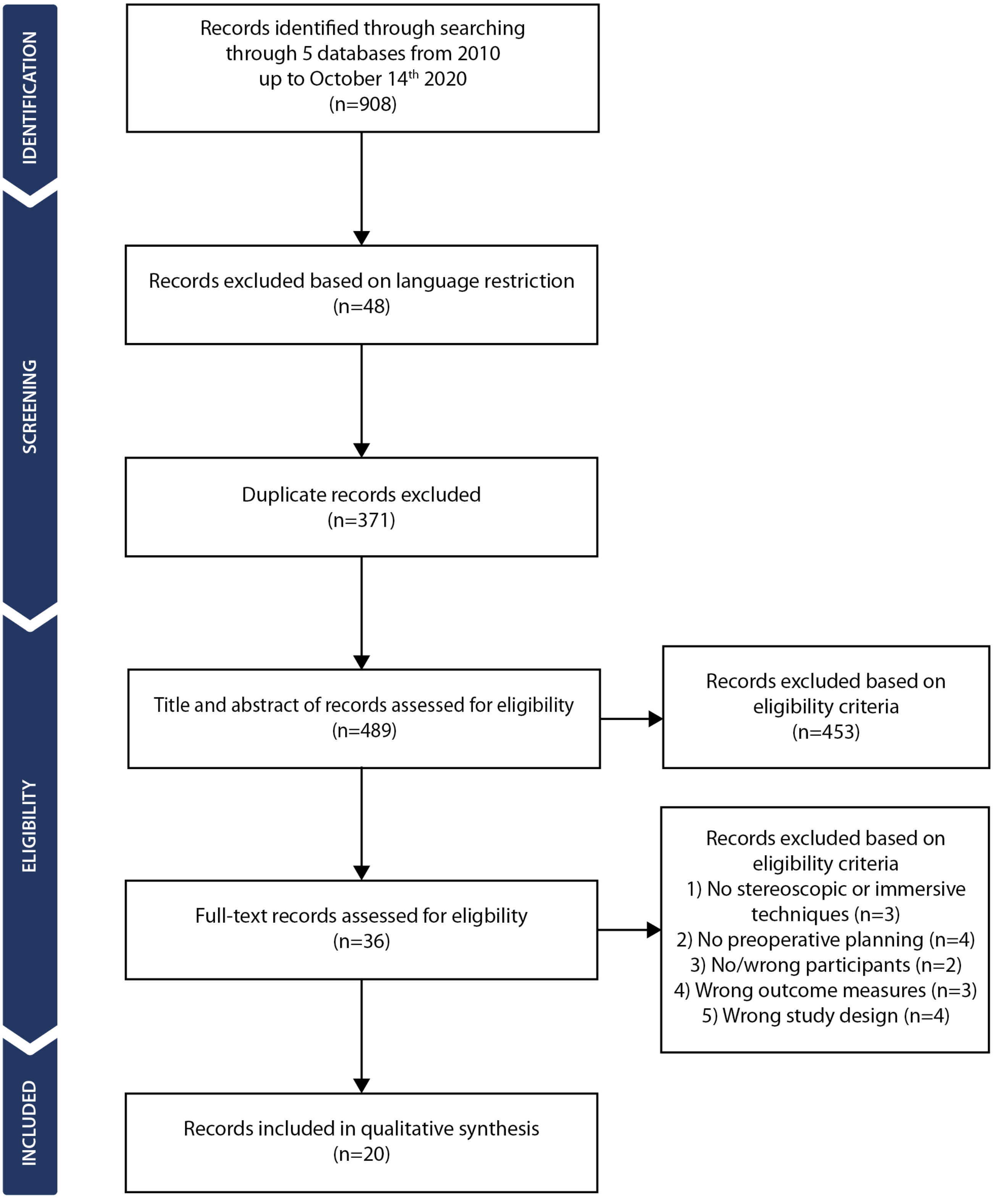

Figure 2.3. The flowchart using the PRISMA method

The printing hardware, time, and costs for printing the models and the printing technique were considered as the most relevant technology characteristics for the physical printed model group. Four studies used printing hardware from Stratasys (Eden Prairie, MN, USA) (13, 16, 19, 21) and two studies used printing hardware from Shanghai Union Technology (Shanghai, China) (7, 15). With several special printing techniques, such as stereolithography and powder binder jetting, all studies reported on successfully generated tactile 3DP objects that have been physically investigated. Von Rundstedt et al (2017) created 3DP models that matched human tissue mechanical properties with a technique from the company Lazarus 3D (Houston, TX, USA). Specific technology related details (costs and printing time) were not described (20). The manufacturing costs of 3DP models varied within a range from a minimum of $15 in the study of Hojo et al (2020) to a maximum of $1200 in the study of Yang et al (2019). The time it took to physically print the 3D models varied from a minimum of 4-9 hours in the study of Komai et al (2016) to a maximum of 4-5 days in the study of Wellens et al (2019). However, most studies reported a time which was in the range of approximately 1 day.

The digital hardware and software used to visualize the stereoscopic patient models and the time it took to create the digital 3D models were considered as the most relevant technology characteristics, specifically for the digital stereoscopic model group. Five studies investigated the use of MR technology during the preoperative planning. They all used the Hololens I (Microsoft, Redmond, WA, USA), which is a wireless HMD with a stereo see-through display (Figure 1). This technology provides its user with a visualization of 3D reconstructed models as holograms embedded in the real physical world (22). The fixed purchase costs for the Hololens I are between $3000 and $5000 (14). However, no variable costs apply to this device.

Shirk et al (2019) used a relatively simple VR technology, the Google Cardboard HMD (Alphabet, Mountain View, CA, USA). The functionalities of this technology were relatively limited when compared to the Hololens I, however this technology costs only $15. For the Google Cardboard, smartphones running a web-based application were needed to visualize the 3D models (23).

The Dextroscope workstation (Volume Interactions, Singapore) with its corresponding Liquid-crystal-display (LCD) shutter glasses (Stereographics, San Rafael, CA, USA)

and 3D reconstruction software RadioDexter (Volume interactions, Singapore) was used in three studies as HD technology (24-27). With the Dextroscope, one can perceive the 3D graphical objects stereoscopically wearing LCD shutter glasses and interact with them using virtual tools (25). Antonelli et al (2019) investigated the application of the zSpace workstation (zSpace, San Jose, CA, USA) combined with passive glasses and a stylus.

Outcome measures

Intra- and postoperative outcomes

The results from the five studies that compared intra- and postoperative outcomes between 3DVTs, 3D-on-2D groups and non-3D groups are summarized in Table 2 (7, 12, 17, 21, 23, 28) and discussed in more detail in this section. Komai et al (2016) reported a significantly shorter intraoperative ultrasound time of 3.3 minutes (3DVT group) compared to 6.3 minutes (non-3D group) (p=.021).

Liu et al (2019) showed that the operating time of 133.0 [35.7] minutes in the non-3D group was significantly longer than the operating time in the 3D-on-2D (p=.024) and 3DP group (p=.008), 115 [37.2] and 111 [36.2] minutes respectively. Additionally, a significantly increased estimated blood loss of 106.3 [70.8] mL in the non-3D group was reported compared to the estimated blood loss in the 3D-on-2D (p=.019) and the 3DP group (p=.009), 75.1 [57.4] and 69.3 [50.9] mL respectively. Nevertheless, there was no significant difference seen between the 3D-on-2D and the 3DP groups in operating time (p=.609) and estimated blood loss (p=.696). Five patients in the non-3D group were converted to thoracotomy or lobectomy due to vascular injury against 1 patient in the 3D-on-2D group and no patients in the 3DP group.

Qiu et al (2020) showed that for complex anatomical partial lobectomy, the operating time of 99.6 [21.7] minutes (3DP group) was significantly shorter than the operating time of 116.1 [30.7] and 125.1 [23.6] minutes in the 3D-on-2D (p=.01) and the non-3D group (p=.<.001), respectively. Additionally, the estimated blood loss of 12.9 [7.8] mL measured in the 3DP group was significantly less than the estimated blood loss of 20.9 [12.2] and 18.2 [12.2] mL measured in the 3D-on-2D (p=.07) and the non-3D (p=.009) groups respectively. No complications were seen in the 3DP group, 3 in the 3D-on-2D group and 1 in the non-3D group.

Li et al 2020 showed that for the pre- and intraoperative application of the Hololens I compared with a non-3D group there was a significantly shorter operating time of 60.7 [10.4] vs 98.4 [11.7] minutes (p<.001), shorter warm ischemia time (WIT) of 12.5 [1.2] vs 20.3 [0.9] minutes (p<.001) and less estimated blood loss of 15.5 [9.5] vs 45.9 [10.1] mL (p<.001). Again, no significant difference between postoperative complications was reported.

Lastly, Shirk et al (2019) reported a significantly shorter operating time of 141 [120, 165] minutes, shorter arterial clamp time of 13.2 [11.5, 15.2] and less estimated blood loss of 133 [92, 193] cc in the VR group against an operating time of 201 [174, 232] minutes (p<.0001), clamp time of 17.4 [14.9, 20.3] minutes (p=.0274) and an estimated blood loss of 259 [174, 386] cc (p=.0233) in the non-3D group. These results were corrected for the differences in experience level of surgeons and case complexity. No complications were seen in the VR group. However, two complications (1 vascular injury and 1 bowel injury) and three positive tumor resection margins were seen in the non-3D group.

Questionnaire outcomes

The results from the eleven studies that conducted questionnaires regarding the utility, experience, usefulness, anatomical understanding, or the surgical strategy of 3DVTs used in the preoperative planning are extensively described in Table 3 (4, 5, 13, 14, 17, 18, 25, 26, 28-30). Qiu et al (2020) showed that 88% of 59 surgeons who completed the questionnaire reported on a better understanding of the thoracic segmental anatomy with 3DP models than with the 3D-on-2D models, 7 surgeons were neutral. In addition, 81.4% of the same group of surgeons agreed that 3DP models were useful for better communication with colleagues. Antonelli et al (2019) also investigated the inter-observer agreement which showed a good agreement for the HD group (k>0.6) compared to a poor agreement for the non-3D group (k<0.6)

Performance assessment outcomes

The results from the eight studies that assessed the performance of surgeons regarding their anatomical understanding, resection times, surgical strategy and planning times are described and provided in Table 4 (4, 9, 13, 15, 16, 19, 20, 27). Three studies reported significantly reduced planning times where 3DP (n=2) and HD (n=1) were compared to a non-3D group (4, 16, 19). However, Incekara et al (2018) reported a significantly larger evaluation time with the use of MR technology compared with no technology et al.

Marconi et al (2017), Yang et al (2017) and Yang et al (2019) showed a significantly higher performance in the anatomical understanding. Their performance was tested in a group of 30 evaluators (mixed experience), another group of 30 evaluators (mixed experience) and a group of 45 surgical residents, respectively. Shi et al (2014) reported that based on visual assessment and tumor diameter measurements were not significantly different (p>.05) in the virtual and intraoperative data for anatomical structures. However, this study only included 1 surgeon.

Von Rundstedt et al (2017) highlighted that no significant difference was seen when the volumes of resected tumors of their human tissue matching 3DP model was compared with the 3D-on-2D model resection and the actual surgery volumes (P=.98).

Yang et al (2019) showed a significantly improved surgical strategy accuracy of 57% (3DP group) compared to both the 25% (3D-on-2D) and 25% (non-3D) group (p<.001). Additionally, Wake et al (2017) reported the percentage of decisions made in the 3DP and the non-3D group that matched with the decisions made during the actual procedure. They reported following preoperative decisions: partial or radical nephrectomy (100% 3DP vs 92.7% non-3D), open or robotic approach (81.5% 3DP vs 77.8% non-3D), retroperitoneal or transperitoneal approach (55.6% 3DP vs 59.4% non-3D) and clamping strategy (85.2% 3DP vs 81.5% non-3D).

Table 2.2. Intra- and postoperative outcomes

Author (Year)	Type of outcomes	Mean [SD] 3DVT	Mean [SD] 3D-on-2D	Mean [SD] non-3D	P-value (3DVT vs non-3D)	P-value (3D-on-2D vs non-3D)	P-value (3DVT vs 3D-on-2D)
Komai, Y. et al. – 2016 (21)	Intraoperative ultrasound time, minutes	3.3 [-]	-	6.3 [-]	**.021 ***	-	-
Liu, X. et al. – 2019 (7)	Operating time, minutes	111 [36.2]	115 [37.2]	133.0 [35.7]	**.008 ***	**.024 ***	.609
	Estimated blood loss, mL	69.3 [50.9]	75.1 [57.4]	106.3 [70.8]	**.009 ***	**.019 ***	.696
	Hospital stay, days	4.4 [1.9]	4.5 [1.7]	5.1 [1.0	**.004 ***	**.028 ***	.390
	Chest tube duration, days	3.4 [1.8]	3.4 [1.6]	3.9 [1.6	.170	.200	.878
	Conversions to thoracotomy due to arterial complications, n	0	1	5	.152	.373	1.0
Qiu, B. et al. – 2020 (17)	Operating time complex segmentectomy, minutes	99.6 [21.7]	116.1 [30.7]	125.1 [23.6]	**<.001***	**.04***	**.01***
	Estimated blood loss, mL	12.9 [7.8]	20.9 [12.2]	18.2 [12.2]	**.02***	**.07***	**.001***
	Hospital stay, days	4.5 [1.6]	4.7 [1.5]	5.0 [1.5]	.174	.21	.54
	Chest tube duration, days	4.5 [1.6]	4.1 [1.5]	4.1 [1.4]	.16	.75	.13
	Postoperative drainage, mL	608.9 [369.5]	650 [435]	566.3 [401.9]	.59	.11	.63
	Complications, n	0	3	1	-	-	-
Li, G. et al. – 2020 (28)	Operating time, minutes	60.7 [10.4]	-	98.4 [11.7]	-	**<.001***	-
	Warm ischemia time	12.5 [1.2]	-	20.3 [0.9]	-	**<.001***	-
	Estimated blood loss, mL	15.5 [9.5]	-	45.9 [10.1]	-	**<.001***	-
	Hospital stay, days	6.8 [1.0]	-	7.0 [0.9]	-	.296	-
	Preoperative creatinine, mol/L	106.3 [12.4]	-	88.5 [13.3]	-	.121	-
	Postoperative creatinine, mol/L	106.3 [12.4]	-	11.5 [14.7	-	.059	-
	Postoperative complications	1	-	3	-	.312	-
Shirk, J. D. et al. – 2019 (23)	Operating time[a], minutes	141 [120, 165]	-	201 [174, 232]	-	**<.0001***	-
	Estimated blood loss[a], cc	133 [92, 193]	-	259 [174, 386]	-	**.0274***	-
	Clamp time[a], minutes	13.2 [11.5, 15.2]	-	17.4 [14.9, 20.3]	-	**.0233***	-
	Hospital stay >2 days vs 0-2 days[b], Odds ratio	-	-	5.1 [1.0, 26.4]	-	**.0498***	-

(*P<0.05, a back transformed from linear regression controlling for nephrometry score, surgeon and resident, b odds ratio from logistic regression controlling for nephrometry score and surgeon).

Table 2.3. Questionnaire outcomes

Author - Year	Type of questionnaire	Evaluators	Findings [SD]
Hojo, D et al. – 2020 (18)	Subjective utility (Likert scale 1-5)	30 surgeons	- Overall anatomical understanding: 4.68 [0.58]. - Spatial anatomical comprehension: 4.83 (3DP) compared to 4.36 (3D-on-2D) (P<.001). - Ease of use: 4.60 (3DP) compared to 4.20 (3D-on-2D) (p<.0015).
Porpiglia, F et al. – 2018 (29)	Utility (Likert scale 1-10)	144 attendees (47 expert radiologists, 39 urologists and 58 residents in urology)	- Surgical planning 7-9/10. - Anatomical accuracy 10/10. - Role of technology in surgical training 9/10.
Qiu, B. et al. – 2020 (17)	Usefulness	59 surgeons	- 52 (88%) of the surgeons agreed that the 3DP models provided a better understanding of the thoracic segmental anatomy than 3D-on-2D. 7 (12%) surgeons were neutral. - 52 (88%) of surgeons agreed or strongly agreed that 3DP models were useful for better communications with patients or other colleagues. - 10 (16.9%) surgeons were neutral about popularizing 3DP models as a routine tool for complex procedure due to costs. - 48 (81.4%) surgeons agreed or strongly agreed that the model might help to diminish potential surgical outcomes. - 30 (50.9%) surgeons strongly agreed that 3DP models were more convenient than 3D-on-2D during operation. Overall average satisfaction 3DP models 8.0/10.
Wake, N. et al. – 2017 (13)	Usefulness and surgical strategy	3 experienced urologists	All three surgeons reported that: - The 3DP helped with comprehension of anatomy, - The 3DP helped with regards to decisions on surgical approach, - Increased their confidence that they correctly planned the procedure.
Zhang, Y. et al. – 2016 (30)	Usefulness (1-10 rating scale)	4 experienced urologists	- Satisfaction overall usefulness 7.8 [0.7]. - Help in planning and training 8.0 [1.1]. - Realism (6.0 [0.6] - 7.8 [1.0])
Wellens, L. M. et al. – 2019 (14)	Anatomical understanding (Likert scale)	7 oncology surgeons	- 3DP and MR, respectively, led to better assessment of the tumor (p=.008 and p=.002), arteries (p=.002 and p<.001), veins (p<.001 and p<.001)) and urinary collection structures (p<.001 and p<.001) compared to conventional imaging. - No significant difference between 3DP and MR.
Checcucci, E. et al. – 2019 (5)	Usefulness (Likert scale 1-10)	172 attendees	- Surgical planning 8/10 - Anatomical accuracy 9/10 - Satisfaction surgical planning 9/10 - Understanding surgical complexity 9/10
	Mixed Reality Room experience questionnaire	90 participants (40 expert urologists, 20 young urologists, and 30 urology residents)	- 64.4% of the participants changed clamping and surgical strategy (MR group) compared to 44.4% (non-3D group) changed clamping and surgical strategy (p<.001)
Li, G. et al. – 2020 (28)	Usefulness	2 senior surgeons	- Value of MR in operative plan formulation, intraoperative navigation, remote consultation, teaching guidance, and doctor-patient communication were higher in the MR group than in the non-3D (all p<.001).
Stadie, A. T. et al. – 2013 (25)	Usefulness and surgical strategy Dextroscope	20 surgeons	- Change in surgical strategy compared with planning with non-3D in 53 of 208 cases. - Good or very good improvement for preoperative spatial understanding (93.3%). - Preoperative planning of craniotomy size and location (83.1%). - Intraoperative spatial orientation (74.5%). - Intraoperative confidence (74.6%).
	Expectations Setred system	Surgeons in 33 cases	- Easy establishment of surgical strategy n=33/33. - Better visualization of pathology and surrounding anatomic structures (n=9/8). - Serving as navigation backup solution (n=24/24).
Wang, S. S. et al. – 2012 (26)	Experience	11 surgeons	- 10/11 surgeons using HD experienced differences between the 3D reconstruction and the actual anatomy during surgery but that the model helped understanding the anatomy. - 9/11 surgeons thought HD displayed 3D reconstructions were superior to 3D-on-2D but there was still a need for other images to be used in combination with the 3DVT.
Antonelli, A. et al. – 2019 (4)	Clinical utility (Likert Scale 1-5)	7 urologists	- 7 raters reported to agree or completely agree (4/5) with statements regarding utility except statement related to prevention of complications where 4/7 raters reported that they did not agree.
	Inter-observer agreement	7 urologists	- Poor agreement with k<0.6 (non-3D group) compared to good agreement k>0.6 (HD group) for almost all anatomical details considered.

Table 2.4. Performance assessment outcomes

Author - Year	Type of performance assessment	Evaluators	Score assessment [SD]
Marconi, S. et al. – 2017 (19)	Anatomical understanding (%)	10 medical students, 10 surgeons and 10 radiologists	- Correct answers: 45.5% [4.6] (non-3D), 53.4% [4.6] (3D-on-2D) and 53.9% [4.14] (3DP). Significant difference between non-3D and both 3D-on-2D and 3DP group (p<.001). - No significant difference between 3D-on-2D and 3DP group (p=.676)
	Planning times (minutes)	10 medical students, 10 surgeons and 10 radiologists	- Mean time spent 127.04 [35.91] seconds (non-3D), 70.8 [28.18] seconds (3D-on-2D) and 60.67 [25.5] seconds (3DP). - Significantly lower time spent in both 3D-on-2D and 3DP group compared to the non-3D group (was significantly lower than the time spent on non-3D **(p<.001).**
Von Rundstedt, F. C. et al. – 2017 (20)	Resection times (minutes)	1 surgeon	- Mean resection times human tissue like 3DP model and patient are 6:58 vs 8:22 minutes (p=.162).
	Resection volumes	1 surgeon	- Mean resected tumor volumes between 3D-on-2D, 3DP and actual patient are 38.88 vs 38.50 vs 41.79 mm3 (p=.98).
Wake, N. et al. – 2017 (13)	Surgical strategy (% of planned decisions matched with actual surgery)	3 experienced urologists	- Partial or radical nephrectomy: 100% 3DP - 92.7% non-3D. - Open or robotic: 81.5% 3DP - 77.8% non-3D. - Retroperitoneal or transperitoneal approach: 55.6% 3DP - 59.4% non-3D. - Clamping: 85.2% 3DP - 81.5% non-3D.
Yang, T. et al. – 2017 (15)	Anatomical understanding (%)	30 evaluators (10 students, 10 residents, 10 surgeons)	- Recognitions of all three vasculatures simultaneously was 46.67% (non-3D), 73.33% (3D-on-2D), 83.33% (3DP), respectively **(p=.007).**
Yang, T. et al. – 2019 (16)	Anatomical understanding tumor location (max 100 points)	45 surgical residents	- Mean score of 34.50 (non-3D), 55.25 (3D-on-2D), 80.92 (3DP). 3DP group significant higher scores compared to non-3D and 3D-on-2D **(p<.001).** - No significant difference between non-3D and 3D-on-2D.
	Surgical strategy (%)	45 surgical residents	- Mean accuracy was 25% (non-3D), 25% (3D-on-2D), 57% (3DP). - 3DP group significantly improved the accuracy of **(p<.001)** compared to non-3D and 3D-on-2D.
	Planning times (seconds)	45 surgical residents	- Mean time spent on assigning tumor location 286 seconds (non-3D), 223 seconds (3D-on-2D) for 3DP and 93 seconds (3DP). - 3DP group significantly less time (p<.005) compared to non-3D and 3D-on-2D.
Incekara, F. et al. – 2018 (9)	Planning times (minutes)	Authors with prior Hololens experience who attended surgery	- Mean 5 minutes and 20 seconds [1 minute and 20 seconds] (MR group) **(p<.001)** compared to 4 minutes 25 seconds [1 minute 20 seconds] (non-3D).
Shi, J. et al. – 2014 (27)	Anatomical understanding	1 surgeon	- Virtual and intraoperative data for anatomical structures were not significantly different based on subjective visual assessment and tumor diameter measurements (p>.05).
Antonelli, A. et al. – 2019 (4)	Planning times (minutes)	7 urologists	- Significant difference with a mean 1.7 minutes [0.8 minutes] (HD) compared to a mean of 3.4 minutes [1.7] (non-3D group) **(p<.001).**

Discussion

In this systematic review, the added values of 3DVTs applied during the preoperative planning of complex oncological resection surgery were identified by studying the included literature. The most relevant findings regarding the clinical outcomes, the performance assessments and the questionnaires are discussed in this section. Additionally, the techniques are compared and the hurdles of the contemporary 3DVTs are discussed.

Improved intra- and postoperative clinical outcomes

Ultimately, the application of 3DVTs in the preoperative planning would significantly improve the intra- and postoperative clinical outcomes of the procedures with parameters such as operation time, estimated blood loss and a lower complication rate of the performed tumor resection procedures. Five studies reported on the comparison of the clinical outcomes. Liu et al (2019) showed in a high-quality study that the operating time and the estimated blood loss in the 3D-on-2D and the 3DP group were significantly less than in the non-3D group during thoracoscopic pulmonary segmentectomies.

Additionally, Shirk et al (2019) showed a significantly shorter operating time, shorter arterial clamp time and a lower estimated blood loss was reported compared to the non-3D group after controlling for the experience of surgeons and case complexity. The author claimed that the vascular injury, that was seen in the non-3D group, could have been prevented with the use of VR technology. Shirk et al (2019) also hypothesized that investigating the tumor in depth in VR could results in surgeons having more confidence attaining negative tumor margins. This could explain why three positive tumor resection margins were seen in the non-3D group and no positive margins in the VR group. Nevertheless, these statements of Shirk et al (2019) were not supported with statistically relevant differences between the groups. Therefore, further research should be done to prove if the use of VR technology could significantly lower the vascular complication rate and the amount of positive tumor resection margins.

3DVTs would presumably have a more added value in visualizing the anatomical relationships for relatively complex procedures. Qiu et al (2020) studied the use of different personalized 3DP models during anatomical partial lobectomy and confirmed that 3DVTs have more added value in complex procedures than in simple procedures. In simple APL, there was no significant difference reported between the non-3D group, the 3D-on-2D group and the 3DP group. However, the results for complex APL were more remarkable, since the operating time and the estimated blood loss of the 3DP group were significantly less than in the 3D-on-2D and the non-3D group.

Furthermore, Li et al (2020) evaluated the clinical value of MR-assisted (Hololens I) surgical navigation assisted by the Hololens I in laparoscopic nephrectomy. This study of showed a significantly shortened operating time, warm ischemia time (WIT) and reduced estimated blood loss. However, this study focussed on both preoperative and intraoperative application of Hololens and therefore it cannot be concluded that this statistical difference was due to the application of 3DVTs in the preoperative planning. Despite this, the study still shows that the application of MR technology significantly improves the clinical outcomes in laparoscopic nephrectomies.

Performance assessments & questionnaires

Understanding the complex spatial anatomy

The complexity of cancer resection surgery is highly variable between patients and depends on several patient factors, on the size and location of the tumor and its interaction with vital anatomical structures. Nine studies (4, 5, 13, 14, 17, 18, 25, 26, 29) showed with questionnaires and four studies (15, 16, 19, 24, 27) with performance assessments a better spatial understanding of the complex patient-specific anatomy with the use of 3DVTs and therefore better understanding of interactions of vital structures with the tumor.

Li et al (2020) stated that MR technology can enable surgeons to study the patient-specific anatomy naturally, intuitively, stereoscopically, and comprehensively and at the same time can reduce the difficulty of identifying the complex spatial relationships of the critical structures with the tumor tissue.

Marconi et al (2020) highlighted a significant improved performance of participants with mixed experience evaluating tumor size estimates, vascular details, and spatial relationships with a 3DP and 3D-on-2D group compared with the non-3D group. However, Marconi et al (2020) did not correct for the time that surgeons spent on the preoperative planning. Once could expect that surgeons will have a better anatomical understanding if they spend more on studying the specific patient anatomy.

Yang et al (2019) recorded, in contrast to Marconi et al (2020), the time spent on assigning the tumor location. Performance assessments on surgical residents showed significant less time spent on assigning tumor location while obtaining significantly higher scores on anatomical understanding in the 3DP group compared with a 3D-on-2D and non-3D models.

Qiu et al (2020) showed with their questionnaire regarding the subjective satisfaction that surgeons have a better understanding of the thoracic segmental anatomy with the use of 3DP models compared with 3D-on-2D models. Furthermore, the majority of the surgeons in this study of Qiu et al (2020) agreed that 3DP models were useful for better communication with colleagues. Antonelli et al (2019) highlighted a better agreement among the observers during the interpretation of anatomy and pathology on the HD.

Surgical strategy

There were five studies that, using questionnaires, showed that the use of 3DVTs changed their surgical approach (5, 13, 25, 28, 29). Additionally, two studies assessed the changes in surgical strategy when 3DVTs were applied in the preoperative planning (13, 16). In the study of Checcucci et al (2019), the usefulness of MR technology in aiding preoperative planning for the resection of highly complex renal tumors in nephron-sparing surgery was examined. Substantial parts of the urologist, with mixed levels of experience, changed the clamping strategy and/or the resection approach after studying the 3D model in MR. Even after stratifying for expertise of the participants, the number of modified strategies compared with a more conservative approach remained significant. Nevertheless, it must be considered that their strategy is expected to be more conservative if they need to make the decision in a real patient case to guarantee the safety of the procedure.

In the study of Wake et al (2017) surgeons were assessed on altering preoperative decisions regarding complex partial or radical nephrectomy, open or robotic approach, retroperitoneal or transperitoneal approach and their clamping strategy. Most frequent changes were seen in decisions regarding the retroperitoneal or transperitoneal approach and the use of clamping. For the most complex procedures, surgeons altered their surgical strategy more frequently when they used a 3DP model. Thus, in patients with a high degree of anatomic complexity, the 3DP might be valuable in determining the surgical strategy in the preoperative phase. They indicate that even experienced surgeons may benefit from the application of 3DP patient models in complex nephrectomies. Nevertheless, it should be noted that Wake et al (2017) had a limited sample size in both patients and participants.

Yang et al (2019) showed that the accuracy of the resection proposal in the 3DP group was significantly higher compared to non-3D and 3D-on-2D. However, this study may only point out the usefulness of 3DP in helping the surgical residents to understand the anatomy of liver abnormalities and does not reflect on the performance of experienced surgeons in defining their surgical strategy.

Lastly, Stadie et al (2013) investigated the application of the Dextroscope workstation (HD) during brain cancer resection procedures. A presurgical questionnaire concerning whether the planning session with the Dextroscope workstation led to a change in surgical approach compared with 2D images showed that in approximately a quarter of the cases the planning on the HD resulted in a changed surgical strategy.

Shorter learning curve, more confidence

Regarding educational purposes, Yang et al (2017) reported increased retroperitoneal anatomy understanding for students that used 3DP patient models and increased recognition of the involved vasculature (except for the IVC) for surgical residents. They showed limited advantage for 3DP models over the non-3D group for surgeons and even no advantage over the 3D-on-2D group. In addition, Liu et al (2019) highlighted that 3DP models helped thoracic surgical residents making faster and better preoperative plans. Nevertheless, 3D-on-2D were still difficult to interpret due to immature pulmonary anatomy understanding and inexperienced stereoscopic perception. Liu et al (2019) believes that the use of 3D models on 2D displays will be sufficient for experienced surgeons to get a comprehensive understanding of the anatomy of the patient. Surgeons have an extremely high understanding of the distribution of the most relevant pulmonary arteries, veins, and bronchi in 3D.

Another added value that was reported qualitatively is the use of 3DVTs during the preoperative planning increased the confidence of the surgeon to make the preferred decision and perform the complex resection procedure (13, 17, 25).

Planning times

Finally, three studies reported lower preoperative planning times for the 3DVTs groups compared with the non-3D group (4, 16, 19, 24). The preoperative planning time comprises all time surgeons and other clinicians spend on preparing the surgical resection procedure. The studies that evaluate the planning time only observed the time it took to evaluate the anatomy. In contrast to the results of these three studies, Incekara et al (2018) reported a significantly increased planning time when MR technology is used against a planning time without visualization techniques. However, this deviation of 45 seconds would certainly be acceptable for a preoperative planning setting if neurosurgical planning would be significantly improved.

Comparison techniques

3DVTs versus 3D models on 2D displays

The technological advancements in imaging processing have made it possible to reconstruct the conventional imaging into 3D reconstructions. This translation from 2D to 3D models is according to Marconi et al (2020) the biggest improvement in the anatomical understanding. No significant difference was seen regarding the anatomical understanding between the 3DP and 3D-on-2D group. As mentioned in the introduction, 3D reconstructions displayed on 2D screens come with limitations regarding the real depth perception (5). Consistently, Hojo et al (2020) showed that surgeons did experience a significantly better spatial comprehension. Furthermore, more than half of the surgeons in the study of Qiu et al (2020) agreed that 3DP models are more convenient than 3D models on 2D displays during surgery. Nevertheless, in terms of clinical outcomes, Liu et al (2019) reported no significant difference in operating time and estimated blood loss between the 3DP and 3D-on-2D group.

Physical printed versus digital stereoscopic models

The most important differences between the use of digital and physical patient models are highlighted in this section. First, the interaction between the physical and digital model is completely different. With 3DP models, clinicians interact with real physical objects. In contrast to 3DP models, digital models allow clinicians to interact with objects that does not really exist in the physical world. Komai et al (2016) argued that 3DP models give surgeons a tactile experience. This tactile experience helps them with understanding the actual tumor size and depth. Although MR does not provide a tactile experience yet, it can enable the surgeon to study the anatomy by means of hand gestures and voice commands (28). Li et al (2020) stated that this allows the surgeons to study the patient anatomy naturally, intuitively, and stereoscopically while obtaining a comprehensive understanding of the complex spatial relationships. However, digital stereoscopic models can only be used by means of relatively complex MR, VR and HD technologies. Those technologies come with a learning curve for clinicians while 3DP models can be used and understood instantaneously and does not require experience with the 3DP technology at all.

Wellens et al (2019) stated that MR is an adaptive and interactive technology. Compared with physical printed models, digital (stereoscopic) models can be easily opened, manipulated, and changed in transparency. 3DP models are a static representation of the patient anatomy and cannot be easily manipulated after the model is printed. To improve the visual interaction 3DP models, the use of translucent material is highly recommended (31). Non-transparent materials result in a great limitation in clinical practice since the clinician will be unable to see vessels and nerves inside the tumor. Thorough inspections of the tumor and its relationships with relevant vasculature will improve when using translucent materials certain structures.

Another difference is the time and effort it takes to construct the models. Digital patient models have a relatively short lead team compared with physical models. The reconstruction of the MR model used in Wellens et al (2019) takes approximately 1-2 hours compared to the manufacturing time of printed models which took approximately 4-5 days. This could be an important advantage of digital 3DVTs. In addition, digital techniques are costless after the initial hardware costs (for example HMDs or HDs) except for labor time it requires of the engineers to reconstruct the models. Physical models require costs every printed patient case.

Lastly, digital and physical models differ in potential intraoperative applications. Physical printed models can be easily brought into the operating room for intraoperative inspection. Tactile experience of the relevant anatomical structures appears to be a considerable support during minimal invasive surgery since touch sense is lacking in these types of procedures (19). Qiu et al (2020) reported that placing the 3DP model intraoperatively, accidental injuries of the small vasculature could be minimized which results in a reduced risk of the procedures. They think it might explain why the estimated blood loss in their complex segmentectomy procedures was lower than in the 3D-on-2D and non-3D group. Contrary to physical printed models, the MR devices such as Microsoft's Hololens have a wireless design and creates possibilities for intraoperative use as well. The Hololens could be controlled with simple intuitive hand gestures and voice commands during the procedure while remaining completely sterile.

Hurdles 3D visualization techniques

Although the 3DVTs described in this systematic review show promising added values, it is important to point out the hurdles that limit the implementation in clinical practice. Thirteen studies discussed that further development of the techniques is needed these can be clinically implemented (4, 9, 13-16, 21, 23, 25-28, 30). Especially limited accuracy regarding 3D image processing and surface registration for MR could be further increased (9, 14, 26, 27). Algorithms are used to segment the relevant anatomy on the conventional imaging and reconstruct 3D models. In the study of Wellens et al (2019), the segmentation was done manually by experts. Wellens et al (2019) argued that standardized algorithms are needed to obtain high accuracy in the digital and physical 3D anatomy models. Additionally, standardized segmentation algorithms could potentially save valuable time in the process since does not require the effort and time of expert radiologists to manually segment structures anymore. Moreover, the optimal imaging method, slice thickness, timing for contrast and resolution is key in constructing accurate 3D patient models.

The currently available solutions still come with high costs according to ten studies (Table 7A and 7B in Appendix 2.3) (4, 5, 7, 13, 15-17, 19, 21, 32). Furthermore, ten studies stated that the reconstruction time of the 3DVTs is time and effort consuming (5, 7, 13-19, 32). To avoid wasted costs and time, Qiu et al (2020) proposed that before 3DP technology is applied only on complex APL cases. The patient case should meet certain criteria to qualify as a complex case before the 3DP technique is applied in the preoperative planning. Such criteria to determine complexity would be valuable for other cancer resection procedures as well, since the relatively limited added value of 3DVTs in simple cases may not compensate the time and cost involved.

Incekara et al (2018) investigated the clinical feasibility and the accuracy of the Hololens I for preoperative neurosurgical planning. Their planning process was carried out right before surgery in the operating room. Situational awareness is crucial for safe surgical procedures. When using VR technology, the surgeon would be isolated in a virtual world while being in the operating room. According to the author, this would explain why the role of VR is limited within the field of neurosurgery. However, Incekara et al. (2019) also state that VR would be useful to improve the understanding of patient-specific anatomy in extraoperative environments.

Limitations review

This systematic review has a few limitations. In the first place, the collected data from the included literature was mainly qualitative data and limited quantitative data was available. Unfortunately, in current practice it is still difficult to quantitatively compare the outcomes of various 3DVTs. As expected, many studies used questionnaires as outcome measures regarding the experience, utility, and value of 3DVTs which only gives opinion of surgeons and surgical residents.

An additional limitation of the systematic review is that the interpretation of the results might be biased by the experience and knowledge of the authors. However, the screening, quality assessment and the collection and interpretation was done very carefully according the systematic PRISMA approach.

The included literature was sensitive in several ways to bias which might have influenced the outcomes of the studies. New impressive 3DVTs might implicitly have biased the results of the studies. Surgeons' personal beliefs whether certain technologies would be better than current practice will have especially influenced the subjective questionnaires in some studies. Moreover, the Hawthorne effect may have played a role in multiple studies as well, but particularly in Shirk et al (2019). Surgeons were aware that their surgical performance was measured while using 3DVTs which might introduce this kind of bias (33). The outcomes of Li et al (2020) might be biased as well by this effect. The surgeons knew that the intraoperative parameters were measured and therefore possibly performed relatively better during MR group procedures.

Further research

Ultimately, the application of 3DVTs improves the intra- and postoperative clinical outcomes. Four studies already reported significantly better clinical outcomes in terms of operating time and estimated blood loss. The outcomes regarding the influence of 3DVTs on the complications rate and positive tumor resection margins were in contrast to the operating time and estimated blood loss not supported with any statistically relevant differences. The contemporary literature still provides limited quantitative data regarding these clinical outcomes. However, the application of 3DVTs is increasingly embraced in clinical practice. This allows for more quantitative follow-up research that could provide more statistical evidence regarding the added value and the clinical relevance of the 3DVTs in complex oncological resection surgery.

This review only considered studies that reported on the added value of 3DVTs used during preoperative planning of surgical oncology procedures. Literature also frequently reported on the applications of 3DVTs in four different areas, namely 1) surgical resident training and education, 2) patient understanding and education, 3) real time video broadcasting to experts (only MR) and 4) intra-operative guidance. It would be valuable to generate additional search strategies to research the added values of 3DVTs in these specific areas.

Multiple studies showed that the application of 3DVTs changed the surgical plan. However, it should also be remarked that a changed surgical strategy does not necessarily mean a better surgical strategy. It was not clear in the included studies if the changes in surgical strategy eventually led to improved outcomes of the procedure. Therefore, more research should be done in order to compare the surgical strategies with the real outcome.

Conclusion

This systematic review provides an extensive qualitative overview on the added values of emerging 3D visualization techniques used during the preoperative planning of complex surgical oncology whilst considering the limitations. The application of 3DVTs could reduce the operating time and estimated blood loss in complex surgical procedures. These techniques enable the surgeons with a better spatial understanding of the complex anatomical relationships. Studying these anatomical relationships stereoscopically before the procedure could lead to changed surgical strategies. In addition, surgeons are more confident choosing surgical strategies and performing the resection procedure. Both physical printed and digital stereoscopic models provide new pre- and intraoperative interaction possibilities, that will improve the communication within the surgical team. Further technological development needs to be done to eventually facilitate wide clinical implementation of 3DVTs.

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Appendix 2.2 - Search Strategy

Appendix table 2.5. Database specific search strategies

Pubmed	(("Imaging, Three-Dimensional"[Mesh] OR "3D visual*"[tw] OR "3 D visual*"[tw] OR "Three Dimensional visual*"[tw] OR (("3D"[tw] OR "3 D"[tw] OR "three dimens*"[tw]) AND ("visual*"[tw]))) AND ("Augmented Reality"[Mesh] OR "Virtual Reality"[Mesh] OR "Augmented Reality"[tw] OR "Virtual Reality"[tw] OR "Mixed Reality"[tw] OR "Printing, Three-Dimensional"[Mesh] OR "Three-Dimensional Print*"[tw] OR "3-Dimensional Print*"[tw] OR "3-D Print*"[tw] OR "3D Print*"[tw] OR "Holography"[Mesh] OR "Hologra*"[tw]) AND ((("Neoplasms"[mesh] OR "neoplas*"[tw] OR "cancer*"[tw] OR "carcinoma*"[tw] OR "adenocarcinoma*"[tw] OR "tumor*"[tw] OR "tumour*"[tw] OR "malignan*"[tw] OR "leukemi*"[tw] OR "leukaemi*"[tw] OR "lymphoma*"[tw] OR "onco*"[tw] OR "Medical Oncology"[Mesh]) AND ("surgery"[Subheading] OR "surgery"[tw] OR "surgical procedures, operative"[mesh] OR "surgical*"[tw] OR "operat*"[tw] OR "preoperat*"[tw] OR "intraoperat*"[tw] OR "postoperat*"[tw] OR "surgeon*"[tw] OR "laparoscop*"[tw]))) AND ("Diagnosis"[Mesh] OR "diagnosis"[Subheading] OR "diagnosis"[tw] OR "diagnos*"[tw] OR "Decision Making"[Mesh] OR "Clinical Decision-Making"[Mesh] OR "Decision Making, Computer-Assisted"[Mesh] OR "decision-making"[tw] OR "Planning Techniques"[Mesh] OR "planning"[tw] OR "plan"[tw] OR "plans"[tw] OR "planned"[tw] OR "Spatial Navigation"[Mesh] OR "Patient Navigation"[Mesh] OR "Neuronavigation"[Mesh] OR "navigation"[tw] OR "navigat*"[tw] OR "neuronavigat*"[tw] OR "treatment selection"[tw] OR "workup"[tw] OR "diagnostic workup"[tw] OR "treatment planning"[tw])) AND (english[la] OR dutch[la])
Embase	((exp "three-dimensional imaging"/ OR "3D visual*".mp OR "3 D visual*".mp OR "Three Dimensional visual*".mp OR (("3D".mp OR "3 D".mp OR "three dimens*".mp) AND "visual*".mp)) AND (exp "Augmented Reality"/ OR exp "Virtual Reality"/ OR "Augmented Reality".mp OR "Virtual Reality".mp OR "Mixed Reality".mp **OR** exp "three dimensional printing"/ OR "Three-Dimensional Print*".mp OR "3-Dimensional Print*".mp OR "3-D Print*".mp OR "3D Print*".mp **OR** "Holography"/ OR "Hologra*".mp) AND (((exp "Neoplasm"/ OR "neoplas*".mp OR "cancer*".mp OR "carcinoma*".mp OR "adenocarcinoma*".mp OR "tumor*".mp OR "tumour*".mp OR "malignan*".mp OR "leukemi*".mp OR "leukaemi*".mp OR "lymphoma*".mp OR "onco*".mp OR "Medical Oncology"/) AND ("su".fs OR "surgery".mp OR exp "surgery"/ OR "surgical*".mp OR "operat*".mp OR "surgeon*".mp **OR** "preoperat*".mp OR "intraoperat*".mp OR "postoperat*".mp **OR** "laparoscop*".mp))) AND (exp "Diagnosis"/ OR "di".fs OR "diagnosis".mp OR "diagnos*".mp OR exp "Decision Making"/ OR exp "Clinical Decision Making"/ OR "decision-making".mp OR *"Planning"/ OR "planning".mp OR "plan".mp OR "plans".mp OR "planned".mp OR exp "Spatial Orientation"/ OR exp "Neuronavigation"/ OR "navigation".mp OR "navigat*".mp OR "neuronavigat*".mp **OR** "treatment selection".mp OR "workup".mp OR "diagnostic workup".mp OR "treatment planning".mp OR "treatment planning"/)) NOT (conference review or conference abstract).pt AND (english OR dutch).la
Web of Science	(ts=("three-dimensional imaging" OR "3D visual*" OR "3 D visual*" OR "Three Dimensional visual*" OR (("3D" OR "3 D" OR "three dimens*") AND "visual*")) AND ts=("Augmented Reality" OR "Virtual Reality" OR "Augmented Reality" OR "Virtual Reality" OR "Mixed Reality" **OR** "three dimensional printing"/ OR "Three-Dimensional Print*" OR "3-Dimensional Print*" OR "3-D Print*" OR "3D Print*" **OR** "Holography"/ OR "Hologra*") AND ts=((("Neoplasm" OR "neoplas*" OR "cancer*" OR "carcinoma*" OR "adenocarcinoma*" OR "tumor*" OR "tumour*" OR "malignan*" OR "leukemi*" OR "leukaemi*" OR "lymphoma*" OR "onco*" OR "Medical Oncology") AND ("surgery" OR "surgery" OR "surgical*" OR "operat*" OR "surgeon*" **OR** "preoperat*" OR "intraoperat*" OR "postoperat*" **OR** "laparoscop*"))) AND ts=("Diagnosis" OR "diagnosis" OR "diagnos*" OR "Decision Making" OR "Clinical Decision Making" OR "decision-making" OR "Planning" OR "planning" OR "plan" OR "plans" OR "planned" OR "Spatial Orientation" OR "Neuronavigation" OR "navigation" OR "navigat*" OR "neuronavigat*" **OR** "treatment selection" OR "workup" OR "diagnostic workup" OR "treatment planning") NOT DT=(meeting abstract) AND LA=(english OR dutch))
COCHRANE library	(("3D visualisation" OR "3 D visualisation" OR "Three Dimensional visualisation" OR "3D visualization" OR "3 D visualization" OR "Three Dimensional visualization" OR "three-dimensional imaging" OR "3D visual*" OR "3 D visual*" OR "Three Dimensional visual*" OR (("3D" OR "3 D" OR "three dimensional") AND (visualization OR visualisation))) AND ("Augmented Reality" OR "Virtual Reality" OR "Augmented Reality" OR "Virtual Reality" OR "Mixed Reality" **OR** "three dimensional printing" OR "Three-Dimensional Print*" OR "3-Dimensional Print*" OR "3-D Print*" OR "3D Print*" **OR** "Holography" OR "Hologra*") AND ((("Neoplasm" OR "Medical Oncology" OR "neoplasm" OR "cancer" OR "carcinoma" OR "adenocarcinoma" OR "tumor" OR "tumour" OR "malignany" OR "leukemia" OR "leukaemia" OR "lymphoma" OR "oncology" OR "neoplasms" OR "cancers" OR "carcinomas" OR "adenocarcinomas" OR "tumors" OR "tumours" OR "malignancies" OR "leukemias" OR "leukaemias" OR "lymphomas" OR "oncological") AND ("surgery" OR "surgeries" OR "surgical" OR "operation" OR "operations" OR "surgeon" OR "surgeons" **OR** "preoperative" OR "intraoperative" OR "postoperative" **OR** "laparoscopy"))) AND ("Diagnosis" OR "diagnosis" OR "diagnos*" OR "Decision Making" OR "Clinical Decision Making" OR "decision-making" OR "Planning" OR "planning" OR "plan" OR "plans" OR "planned" OR "Spatial Orientation" OR "Neuronavigation" OR "navigation" OR "navigat*" OR "neuronavigat*" **OR** "treatment selection" OR "workup" OR "diagnostic workup" OR "treatment planning")):ti,ab,kw NOT (conference abstract):pt
Emcare	((exp "three-dimensional imaging"/ OR "3D visual*".mp OR "3 D visual*".mp OR "Three Dimensional visual*".mp OR (("3D".mp OR "3 D".mp OR "three dimens*".mp) AND "visual*".mp)) AND (exp "Augmented Reality"/ OR exp "Virtual Reality"/ OR "Augmented Reality".mp OR "Virtual Reality".mp OR "Mixed Reality".mp **OR** exp "three dimensional printing"/ OR "Three-Dimensional Print*".mp OR "3-Dimensional Print*".mp OR "3-D Print*".mp OR "3D Print*".mp **OR** "Holography"/ OR "Hologra*".mp) AND (((exp "Neoplasm"/ OR "neoplas*".mp OR "cancer*".mp OR "carcinoma*".mp OR "adenocarcinoma*".mp OR "tumor*".mp OR "tumour*".mp OR "malignan*".mp OR "leukemi*".mp OR "leukaemi*".mp OR "lymphoma*".mp OR "onco*".mp OR "Medical Oncology"/) AND ("surgery".mp OR exp "surgery"/ OR "surgical*".mp OR "operat*".mp OR "surgeon*".mp **OR** "preoperat*".mp OR "intraoperat*".mp OR "postoperat*".mp **OR** "laparoscop*".mp))) AND (exp "Diagnosis"/ OR "diagnosis".mp OR "diagnos*".mp OR exp "Decision Making"/ OR exp "Clinical Decision Making"/ OR "decision-making".mp OR *"Planning"/ OR "planning".mp OR "plan".mp OR "plans".mp OR "planned".mp OR exp "Spatial Orientation"/ OR exp "Neuronavigation"/ OR "navigation".mp OR "navigat*".mp OR "neuronavigat*".mp **OR** "treatment selection".mp OR "workup".mp OR "diagnostic workup".mp OR "treatment planning".mp OR "treatment planning"/)) NOT (conference review or conference abstract).pt AND (english OR dutch).la

Appendix 2.3. Study Characteristics

Appendix table 2.6B. Study characteristics physcial printed model group

Author – year	Technique	Organ	Objective	Intervention	Patients	Evaluators	Comparator	Outcomes	QA
Hojo, D et al. – 2020 (18)	3DP	Pelvic region	To clarify the subjective utility of 3DP pelvic models for lateral pelvic lymph node dissection.	Lateral pelvic lymph node dissection	22 patients (prospective)	30 surgeons	None	Questionnaire evaluated the subjective utility of 3DP models, 3D-CT, and CT for lateral pelvic node dissection.	7.5 (intermediate)
Komai, Y. et al. - 2016 (21)	3DP	Kidney	To report initial experiences with a novel style of 3DP kidney in minimally invasive off-clamp partial nephrectomy.	Minimally invasive off-clamp partial nephrectomy	10 patients (prospective)	Surgeons	None	Intraoperative outcomes and experience questionnaire to surgeons.	5 (low)
Liu, X. et al. – 2019 (7)	3DP	Lung	To explore whether 3DP has a better clinical value for making a preoperative plan than non-3D in thoracoscopic pulmonary segmentectomy.	Thoracoscopic pulmonary segmentectomy	124 patients (32 in 3DP group) (prospective)	Experienced surgeons	3D-on-2D group and non-3D group	Clinical characteristics of patients, Segmentectomy position and numbers, intraoperative and postoperative outcomes.	9 (high)
Marconi, S. et al. – 2017 (19)	3DP	Spleen, Kidney, Pancreas	To validate the preoperative use of 3DP anatomical models in patients with solid organs' diseases as a new tool to deliver morphological information.	Laparoscopic splenectomy, nephrectomy, or pancreatectomy	15 patients (prospective)	10 medical students, 10 surgeons and 10 radiologists	3D-on-2D group and non-3D group	Questionnaire about anatomical understanding and the preoperative planning of the procedure.	7.5 (intermediate)
Porpiglia, F et al. – 2018 (29)	3DP	Prostate and kidney	To test face and content validity of 3DP models used before robot-assisted prostate cancer and nephron-sparing surgery.	Robot-assisted radical prostatectomy and minimally invasive partial nephrectomy during an international urological event	18 patients (prospective)	144 attendees (47 expert radiologists, 39 urologists and 58 residents in urology)	None	Questionnaire about the use and application of the 3DP models.	4 (low)
Qiu, B. et al. – 2020 (17)	3DP	Lung	To estimate the avail of 3D reconstruction and personalized 3DP model in anatomical partial lobectomy.	Anatomical partial lobectomy	298 patients (31 in 3DP group) (retrospective)	59 surgeons	3D-on-2D group and non-3D group	Subjective satisfaction questionnaires and intraoperative indicators including operation time, blood loss, postoperative drainage, chest tube duration, postoperative hospital stay, and complications.	8 (high)
Von Rundstedt, F. C. et al. – 2017 (20)	3DP	Kidney	To describe the experience using patient-specific tissue-like kidney models created with advanced 3DP technology for preoperative planning and surgical rehearsal prior to robot-assisted laparoscopic partial nephrectomy.	Robot-assisted partial nephrectomy	10 patients (prospective)	1 surgeon	3D-on-2D and non-3D group	Resection times and tumor volumes and morphology.	7.5 (intermediate)
Wake, N. et al. – 2017 (13)	3DP	Kidney	To determine whether patient-specific 3DP renal tumor models derived from MRI change preoperative planning decisions made by urological surgeons in preparation for complex renal mass surgical procedures.	Nephrectomy	74 (patients (retrospective)	3 experienced urologists	non-3D group	Questionnaire regarding planned surgical approach.	7 (intermediate)
Yang, T. et al. - 2017 (15)	3DP	Kidney	To investigate whether 3DP model can help to improve understanding of surgical anatomy of retroperitoneal tumors.	Retroperitoneal resection surgery	1 patient (retrospective)	30 evaluators (10 students, 10 residents, 10 surgeons)	3D-on-2D group and non-3D group	The identification of vasculatures important for the tumor resection by participants.	6.5 (intermediate)
Yang, T. et al. – 2019 (16)	3DP	Liver	To investigate the impact of 3DP technology on the understanding of surgical liver anatomy.	Liver segmentectomy or hepatectomy	4 patients (prospective)	45 surgical residents	3D-on-2D group and non-3D group	Tumor assignment, surgical resection proposal and time spent on assignment.	7 (intermediate)
Zhang, Y. et al. – 2016 (30)	3DP	Kidney	To investigate the impact of 3DP on the surgical planning, potential of training and patient's comprehension of minimally invasive surgery for renal tumors	Laparoscopic partial nephrectomy	10 patients (prospective)	4 experienced urologists	None	Effectiveness questionnaire for surgical planning, training, and patients' comprehension of disease and procedures.	5 (low)
Wellens, L. M. et al. – 2019 (14) *	3DP	Kidney	To assess the added value of personalized 3D kidney models derived from conventional imaging data to enhance preoperative surgical planning.	Nephron-sparing surgery	10 patients (children) (retrospective)	7 oncology surgeons	3DP group, MR group, non-3D group	Questionnaire for the assessment of 4 anatomical structures, the procedure decision and the added value of the approach.	8.5 (high)

(QA = quality assessment; N/A = not available; * = also mentioned in appendix table 2.6B)

Appendix table 2.6B. Study characteristics digital stereoscopic model group

Author - year	Technique	Organ	Objective	Intervention	Patients	Evaluators	Comparator	Outcomes	QA
Wellens, L. M. et al. - 2019 (14) *	MR	Kidney	To assess the added value of personalized 3D kidney models derived from conventional imaging data to enhance preoperative surgical planning.	Nephron-sparing surgery	10 patients (children) (retrospective)	7 oncology surgeons	3DP group, MR group, non-3D group	Questionnaire for the assessment of 4 anatomical structures, the procedure decision and the added value of the approach.	8.5 (high)
Checcucci, E. et al. – 2019 (5)	MR	Kidney	Test the face and content validity of mixed reality and assess the role of 3D holograms in aiding preoperative planning for highly complex renal tumors amendable by nephron-sparing surgery.	Robot-assisted partial nephrectomy during a live event.	6 patients (prospective)	172 attendees and 90 participants (40 expert urologists, 20 young urologists, and 30 urology residents).	non-3D group	MR experience and surgical strategy questionnaire.	8 (high)
Incekara, F. et al. – 2018 (9)	MR	Brain	To offer a proof of concept by testing the clinical feasibility and accuracy of a wearable MR device (Hololens) for preoperative neurosurgical planning.	Brain cancer resection surgery	25 patients (prospective)	Authors with prior Hololens experience who attended surgery	Current practice neuro navigation system	Tumor characteristics, planning time, accuracy in tumor localization.	8.5 (high)
Li, G. et al. – 2020 (28)	MR	Kidney	To evaluate the clinical application value of MR-assisted surgical navigation in laparoscopic nephrectomy.	Laparoscopic partial/radical nephrectomy	100 patients (prospective)	Two senior surgeons	non-3D group	Questionnaire to evaluate the clinical application value of MR-assisted surgical navigation and clinical surgery outcomes.	8.5 (high)
Shirk, J. D. et al. – 2019 (23)	VR	Kidney	To determine whether 3D VR models of patient-specific anatomy improve outcomes in patients undergoing robotic partial nephrectomy.	Robot-assisted partial nephrectomy	60 patients (prospective)	3 experienced surgeons	non-3D group	Operative time, clamp time, estimated blood loss, hospital stay, complications, and margins status between these groups.	8.5 (high)
Shi, J. et al. – 2014 (27)	HD	Skeleton	To investigate orthopaedic periarticular tumor surgery planning and anatomical characteristics using a Dextroscope.	Curettage and artificial bone or bone cement implantation.	10 patients (prospective)	1 surgeon	Actual intraoperative situation	Comparison of the presurgical 3D anatomic reconstructions and intraoperative anatomical characteristics and surgical approach measurement and subjective appearance were compared.	3 (low)
Wang, S. S. et al. – 2012 (26)	HD	Brain	To investigate the value of using a VR system for planning resection of sellar region tumors.	Sellar tumor resection surgery	60 patients (prospective)	11 surgeons	non-3D group	Questionnaire about the surgeons' perceptions on the relationship between the model and actual surgery, the advantages of the model.	5 (low)
Stadie, A. T. et al. – 2013 (25)	HD	Brain	To report experiences with 2 VR systems used for planning neurosurgical operations.	Brain cancer resection surgery	208 patients in Dextroscope and 33 patients in Setred group (prospective)	20 surgeons	None	Questionnaire regarding the value of surgery planning preoperatively and postoperatively.	6 (intermediate)
Antonelli, A. et al. – 2019 (4)	HD	Kidney	Evaluate the differences in the perception of renal anatomy between holographic reconstruction versus CT in patients who are candidate to PN.	Robot-assisted Partial nephrectomy	10 patients (prospective)	7 urologists	non-3D group	Inter-observer agreement, evaluation time and questionnaire inquired clinical utility of CT and holographic reconstruction.	7.5 (intermediate)

(QA = quality assessment; N/A = not available; * = also mentioned in appendix table 2.6A)

Appendix 2.4. Technology Characteristics

Appendix table 2.7A. Technology Characteristics physical printed model group

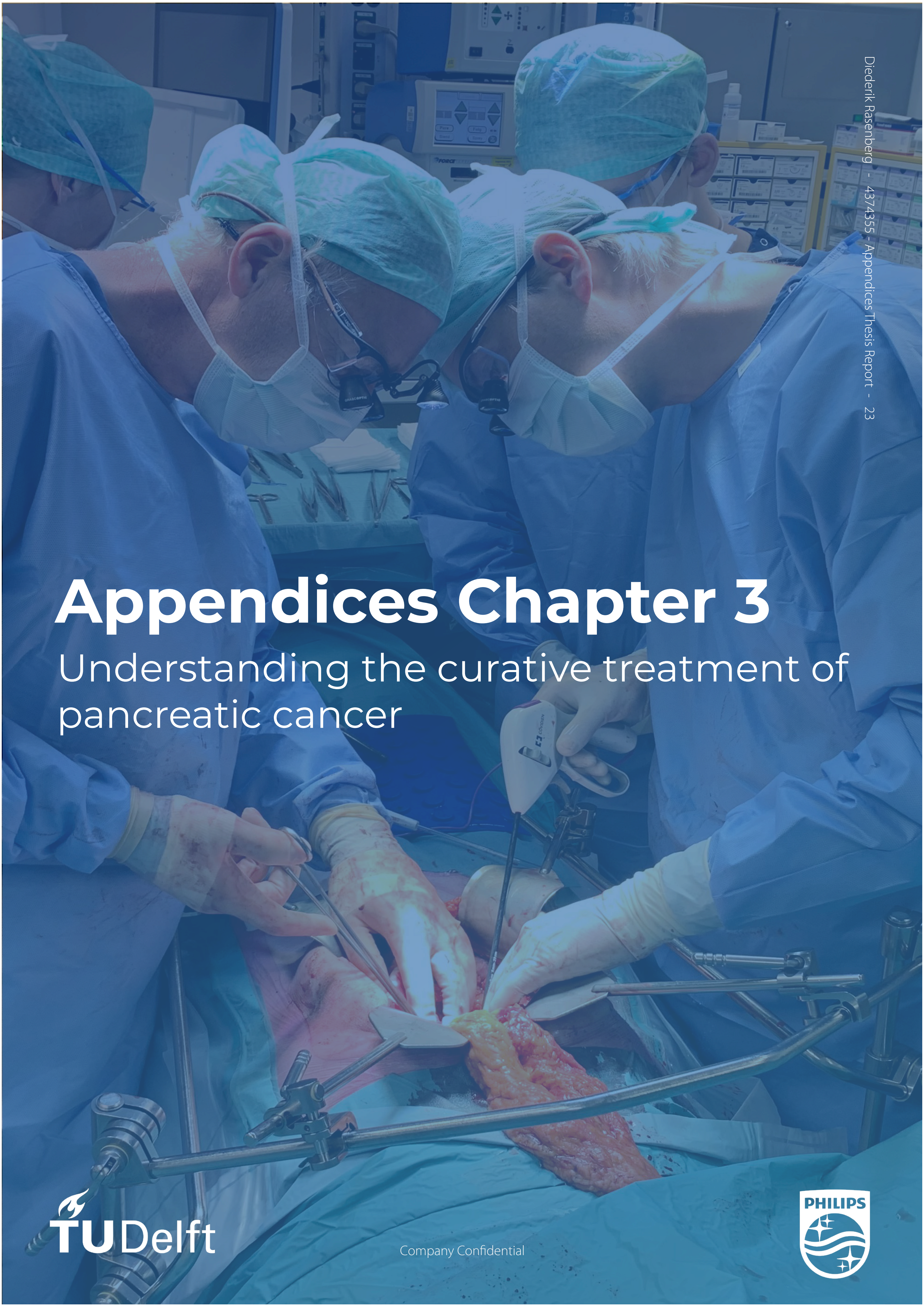
Author - year	Technique	Main imaging modality	Hardware	3D reconstruction software	Time to construct	Costs	Printing time	Printing Technique	Anatomy
Hojo, D et al. – 2020 (18)	3DP	CT	Axiom Dual Extruder (Airwolf 3D, Fountain Valley, CA, USA)	Meshmixer (Autodesk, Venice, CA, USA)	~ 150 minutes	~ 15$	~ 22 - 23 hours	Extrusion based	Internal pudendal, superior gluteal, inferior gluteal, umbilical, superior vesical, inferior vesical, obturator vessels, obturator and sciatic nerve, ureter, piriformis, coccygeus, internal obturator, and levator ani muscles.
Komai, Y. et al. – 2016 (21)	3DP	CT	Objet Connex500 (Stratasys, Eden Prairie, MN, USA)	ZedView (Lexi Co, Tokyo, Japan) Freeform (Geomagic, Rock Hill, SC, USA)	N/A	~ 450$ - 680$	~ 4 - 9 hours	Biotexture Modelling (multimaterial and multicolour)	Vessels, kidney and tumor.
Liu, X. et al. – 2019 (7)	3DP	CT	Lite600HD (Shanghai Union Technology, Shanghai, China)	Mimics (Materialise, Leuven, Belgium)	N/A	N/A	N/A	Stereolithography	Tumor of the target pulmonary lobe, vessels and bronchi.
Marconi, S. et al. – 2017 (19)	3DP	CT	Objet 30 Pro (Stratasys, Eden Prairie, MN, USA)	ITK-SNAP (University of Pennsylvania, Pennsylvania, USA) Paraview (Sandia National Laboratories, Albuquerque, NM, USA)	N/A	~ 150$ - 200$	~ 20 - 30 h	PolyJet technology	Vessels, organ parenchyma and tumor of the pancreas, spleen and kidney
Porpiglia, F et al. – 2018 (29)	3DP	CT/MRI	N/A	M3DICS (Medics 3D, Moncalieri, Torino, Italy)	N/A	N/A	N/A	PolyJet technology Selective Laser Sintering	Prostate: The prostatic glands, tumor of the prostate and the conformation of the neurovascular bundle. Kidney: the arterial vasculature, the kidney shape and the tumor.
Qiu, B. et al. – 2020 (17)	3DP	CT	N/A	Mimics	N/A	N/A	N/A	Stereolithography	Bronchi and blood vessels, the resection region and cutting plane.
Von Rundstedt, F. C. et al. – 2017 (20)	3DP	CT/MRI	Human tissue 3DP (Lazarus 3D, Houston, TX, USA)	3D Slicer (https://www.slicer.org/)	N/A	N/A	N/A	Human tissue mechanical property matching technique	Kidney parenchyma and tumor.
Wake, N. et al. – 2017 (13)	3DP	MRI	Objet Connex500 (Stratasys, Eden Prairie, MN, USA)	Mimics	~ 7 hours	~ 1000$	~ 10 hours	PolyJet technology	Kidney tumor, kidney cortex and medulla, main renal vessels, and ureter.
Yang, T. et al. – 2017 (15)	3DP	CT	RS6000 (Shanghai Union 3D technology Corporation, Shanghai, China)	Mimics	N/A	N/A	N/A	Stereolithography	Left renal vein, the right renal pedicle, the inferior vena cava and the tumor.
Yang, T. et al. – 2019 (16)	3DP	CT	Stratasys J750TM (Stratasys, Eden Prairie, MN, USA)	Mimics	N/A	~ 1200$	N/A	PolyJet technology	The liver, the hepatic veins, the portal vein, the inferior vena cava and the tumor.
Zhang, Y. et al. – 2016 (30)	3DP	CT	LaserCore 5300 (Longyuan Rapid Prototyping Ltd, Beijing, China)	3DMed (Institute of Automation, Chinese Academy of Sciences, Beijing, China)	N/A	~ 150$	~ 3 - 4 days	N/A	Major renal vessels, collecting system (major calyces, pelvis and ureter) and tumor.
Wellens, L. M. et al. – 2019 (14)	3DP	CT/MRI (MRI was preferred)	Zcorp (Materialise NV Technologielaan, Leuven, Belgium)	Mimics	N/A	~ 500$	~ 4 - 5 days	Powder binder jetting	Kidney parenchyma, vessels, kidney urinary collecting system and tumor.

(N/A = not available)

Appendix Table 2.7B. Technology Characteristics digital stereoscopic model group

Author - year	Technique	Main imaging modality	Hardware	3D reconstruction software	Device software	Time to construct	Costs	Anatomy
Wellens, L. M. et al. – 2019 (14)	MR	CT/MRI (MRI was preferred)	Hololens I (Microsoft, Redmond, WA, USA)	Meshmixer (Autodesk, Venice, CA, USA).	Unity (Unity Technologies, San Francisco, CA, USA)	~ 1 - 2 hours	Initial hardware costs ~ 3000$ - 5000$	Kidney parenchyma, vessels, kidney urinary collecting system and tumor.
Checcucci, E. et al. – 2019 (5)	MR	CT	Hololens I	Unity M3DICS (Medics 3D, Moncalieri, Torino, Italy)	weAR	N/A	N/A	Kidney, vessels, calyceal systems and tumors.
Incekara, F. et al. – 2018 (9)	MR	MRI	Hololens I	ITK-SNAP (University of Pennsylvania, Pennsylvania, USA) Meshmixer	VertoStudio and Brainlab (Feldkirchen, Germany).	N/A	N/A	Head surface, brain surface and tumor.
Li, G. et al. – 2020 (28)	MR	CT	Hololens I	Visual3d Medical Technology Development Co (Beijing, China).	N/A	N/A	N/A	Renal tumor, peritumoral tissue structure (including kidney, renal arteriovenous, collecting system, adrenal gland, liver, spleen, intestine, and bones).
Shirk, J. D. et al. – 2019 (23)	VR	CT/MRI	Google Cardboard headset (Alphabet, Mountain View, CA, USA)	N/A	Web-based application	N/A	~ 15$	Renal vessels, kidney parenchyma, collecting system, and tumor(s).
Shi, J. et al. – 2014 (27)	HD	CT/MRI	Dextroscope (Volume Interactions, Singapore) Liquid-crystal-display shutter glasses (Stereographics, San Rafael, CA, USA)	RadioDexter (Volume interactions, Singapore)	RadioDexter	N/A	N/A	Benign periarticular tumors, skeleton, blood vessels and musculature.
Wang, S. S. et al. – 2012 (26)	HD	CT/MRI	Dextroscope and Liquid-crystal-display shutter glasses	RadioDexter	RadioDexter	< 1 hour	N/A	Tumors, bone mass in sellar region, optic nerve, internal carotid artery, circle of Willis, branches, brainstem and ventricles.
Stadie, A. T. et al. – 2013 (25)	HD	CT/MRI	Dextroscope and Liquid-crystal-display shutter glasses Setred system (Setred AS, Oslo, Norway) with MD20-3-D autostereoscopic monitor	RadioDexter	RadioDexter	DS: ≤ 30 minutes Setred: ~ 5 minutes	N/A	Tumors, vessels, ventricles, and bone or skin surface.
Antonelli, A. et al. - 2019	HD	CT	zSpace workstation including passive glasses and stylus (zSpace, San Jose, CA, USA)	Unity	N/A	N/A	N/A	Vessels (vena cava, aorta, main renal vein and artery and branches up to the order shown by the resolution of CT), renal parenchyma, excretory system (ureter, pelvis, calyxes) and renal tumor.

(N/A = not available)



Appendices Chapter 3

Understanding the curative treatment of pancreatic cancer

Appendix 3 - Workflow Analysis Pancreatic Cancer

I. Clinical presentation and diagnotic workup

1. General health tests
General Practitioner

Evaluate medical family history and perform physical examination.

Suspicious results? — No: Patient is sent to other department or home — Yes: 1. Diagnostic health tests

1. Diagnostic health tests
Gastro-Enterologist, Radiologist

a. General health tests.
b. Perform diagnostic CT imaging tests to detect or exclude abnormalities.

2. Review diagnostic imaging
Gastro-Enterologist, Radiologist

Look for clinical suspicion of pancreatic cancer or evidence of dilated pancreatic and/or bile duct.

Suspicious results? — No: **Patient is sent to other department or home** — Yes: 3. Pancreatic imaging protocol

3. Pancreatic imaging protocol
Gastro-Enterologist, Radiologist, HPB surgeon, vascular surgeon, oncologist

a. Pancreatic CT protocol with contrast to further investigate the abnormalities found in the pancreatic region.

b. Pancreatic MRI protocol with contrast to further investigate the abnormalities found in the pancreatic region.

c. Imaging report made by radiologist.

⚠ Peripheral hospitals have less experience in judging complicated cases than expert hospitals.

AI
Segments structures of interest.
Distinguishes between tumor tissue and other tissue.
Determines whether tissue is malignant or benign.
Enlarges accuracy of CT scan interpretation, especially for less-experienced doctors.

4. MDT meeting 1.0
Radiologist, HPB surgeon, vascular surgeon, oncologist, pathologist, radiotherapist

Discuss findings from pancreatic imaging protocol to determine whether or not the cancer is metastatic.

Metastatic? — Yes: 5. Biopsy — No: 5. Pancreatic imaging protocol

5. Biopsy
HPB surgeon, pathologist

Take biopsy with EUS/FNA for confirmation, preferred from a metastatic site.

6. Genetic testing
Pathologist, geneticist

a. Germline testing.
b. MSI and MMR tumor testing.

7. Pancreatic imaging protocol
Radiologist

Chest and pelvic CT.

Metastasis confirmed? — Yes: Arrow to Phase VIII Systematic treatment — No: 5. Pancreatic imaging protocol

5. Pancreatic imaging protocol
Radiologist, HPB surgeon, oncologist

a. Chest and pelvic CT with contrast.

b. **Consider** MRI, in case of clinically indicated, to investigate indeterminate liver lesions.

c. **Consider** PET, in case of high-risk patients, to detect extra pancreatic metastasis. High-risk features include image findings, very highly elevated CA19-9, large primary tumors, large regional lymph nodes, excessive weight loss, extreme pain.

d. Imaging report made by radiologist.

6. Pancreatic scope protocol
Gastro-Enterologist doctor, HPB surgeon

a. **Consider** EUS inspection to guide biopsy of the pancreas, to stage a tumor and detect small lesions.

b. **Consider** ERCP with contrast to take biopsies (brushings) from the common bile duct and for potential stent placement. Stent placements may be considered for symptoms of cholangitis/fever, severe symptomatic jaundice, or if surgery is being delayed for any reason (including neoadjuvant therapy).

7. Blood tests
Pathologist

a. CBC measure for number of red blood cells, white blood cells and platelets, to check for signs of disease and how well organs are working.

b. Liver function tests for measuring liver made chemicals.

c. Test CA 19-9 after biliary drainage, measured before and after neoadjuvant therapy and surgery, to be able to see if the treatment is working or not.

8. Tissue tests
Pathologist

a. **Consider** EUS guiden FNA biopsy, to further investigate the tissue and define if the tissue is malignant or benign.

b. Tissue sample report made by pathologist.

9. Genetic testing
Pathologist, geneticist

a. **Consider** germline testing. Recommended for any patient with confirmed pancreatic cancer.

b. **Consider** MSI and MMR tumor testing. Recommende for any patient with confirmed pancreatic cancer.

Arrow to Phase VIII Systematic treatment

II. Diagnosis and treatment selection

1. MDT meeting 2.0
Radiologist, HPB surgeon, vascular surgeon, oncologist, pathologist, radiotherapist

Discuss all the findings from the pancreatic imaging protocol, pancreatic scope protocol, blood tests, genetic tests and tissue tests with al the clinicians involved.

2. Determine and discuss staging of tumor (TMN) and the resectability
Radiologist, HPB surgeon, vascular surgeon, oncologist, pathologist, radiotherapist

⚠
Difficulties in visualizing the vascular structures and tumor interactions .
No stereoscopic or depth perception in the currently used imaging.
Planning problem in case of borderline resectable.
Periphereal hospitals have less experience in judging complicated cases than expert centres.
Everybody creates different interpretations and translations of the medical imaging to 3D mental model.
Talking about the 3D mental models results in not being sure if they are talking about the same anatomical references.
Longer and more discussions about resectability, taking up valuable time.
In less experienced hospitals or in complex cases, this could result in false positive and false negative decisions about resectability surgery.

AI
Segments structures of interest.
Distinguishes between tumor tissue and other tissue.
Determines whether it is malignant or benign.
Enlarges accuracy of CT scan interpretation, especially for less-experienced doctors.
Determines the resectability of the tumor based on the resectability criteria.

AI and 3D can help reduce the false positive and false negative decisions about resectability surgery.

3D
Getting a better understanding of the patient specific anatomy.
Visualizing the interactions between vascular structures, tumor tissue and other tissue.
Provide stereoscopic / depth view.
Ensures that everybody (e.g. during MDT meeting) is looking at/talking about the same situations and the same anatomical structures.
Gives the clinicians a better and more transparent understanding of AI results.
Improves the explanation of the sitatuation towards the patient and gives a better patient understanding.

a. No mass or diagnosis not confirmed

b. Resectable
- No arterial tumor contact (celiac axis (CA), superior mesenteric artery (SMA) or common hepatic artery (CHA)).
- No tumor contact with superior mesenteric vein (SMV) or portal vein (PV) or ≤ 180 degrees contact without vein contour irregularity.

c. Borderline resectable

Pancreatic head/ucinated arterial:
- Solid tumor contact with CHA without extension to CA or hepatic artery bifurcation allowing for safe and complete resection and reconstruction.
- Solid tumor contact with SMA of ≤180 degrees.
- Solid tumor contact with variant arterial anatomy and presence and degree of tumor contact should be noted, may affect surgical planning.

Pancreatic body/tail arterial:
- Solid tumor contact with CA of ≤ 180 degrees.
- Solid tumor contact with CA of > 180 degrees without involvement of aorta and with intact and uninvolved gastroduodenal artery.

Venous:
- Solid tumor contact with the SMV or PV of > 180 degrees, contact of ≤ 180 degrees with contour irregularity of the vein or thrombosis of the vein, but with suitable vessel proximal and distal to the site of involvement. Allowing for safe and complete resection and vein reconstruction.
- Solid tumor contact with the inferior vena cava (IVC).

d. Locally Advanced

Head/unicinate process arterial:
- Solid tumor contact with SMA >180 degrees.
- Solid tumor contact with the CA > 180 degrees.

Pancreatic body/tail arterial:
- Solid tumor contact of >180 degrees with the SMA or CA.
- Solid tumor contact with the CA and aortic involvement.

Venous:
- Unreconstructible SMV/PV due to tumor involvement or occlusion.

e. Metastatic / unresectable

IIIa. Treatment planning for resectable tumor

1. Pancreatic scope protocol
HPB surgeon, oncologist

a. **Consider** staging laparoscopy in high-risk patients or as clinically indicated, to rule out metastases not detected on imaging (especially for body and tail lesions), or selectively in patients who are at higher risk for disseminated disease. High-risk features include image findings, very highly elevated CA19-9, large primary tumors, large regional lymph nodes, excessive weight loss, extreme pain.

b. EUS guided FNA biopsy **if considering** neoadjuvant therapy.

Neoadjuvant therapy?

Yes

No

2. Neoadjuvant therapy
Oncologist, HPB surgeon, radiologist

Pre-treat the patient with chemotherapy, radiation therapy, targeted terapy, immunotherapy or a combination of these to let the tumor tissue shrink in size.

3. Repeat pancreatic imaging protocol
Radiologist, HPB surgeon, oncologist

a. Chest and pelvic CT with contrast.

b. **Consider** MRI, in case of clinically indicated, to investigate indeterminate liver lesions.

c. Imaging report made by radiologist.

Neoadjuvant therapy changes the relevant structures, making it more difficult to distinghuish the tumor.
Difficult to distinguish tumor tissue and scar tissue in CT scan after neoadjuvant therapy.
No fusion of the pre- and post- neoadjuvant treatment CT/MRI.

AI
Determines/segments what is tumor tissue and scar tissue.
Fusion of medical imaging pre- and post- neoadjuvant treatment can help improve the visualization of the effects of neoadjuvant therapy.

4. Blood tests
Pathologist

Test CA 19-9 after biliary drainage, measured after neoadjuvant therapy, to see if the therapy has worked.

5. Stent placement
HBP surgeon

Consider ERCP with stent placement if clinically indicated for symptoms of cholangitis, fever or severe symptomatic jaundice, or if surgery is being delayed for any reason including neoadjuvant therapy.

IVa. Treatment planning for borderline resectable tumor

1. Pancreatic scope protocol
HPB surgeon, oncologist

a. EUS guided FNA biopsy.

b. **Consider** staging laparoscopy in high-risk patients or as clinically indicated, to rule out metastases not detected on imaging (especially for body and tail lesions), or selectively in patients who are at higher risk for disseminated disease. High-risk features include image findings, very highly elevated CA19-9, large primary tumors, large regional lymph nodes, excessive weight loss, extreme pain.

b. **Consider** ERCP with stent placement if biopsy is found positive for cancer, and/or if clinically indicated for symptoms of cholangitis/fever, severe symptomatic jaundice, or if surgery is being delayed for any reason (including neoadjuvant therapy).

3. Blood tests
Pathologist

Test CA 19-9 after biliary drainage, measured before neoadjuvant therapy, as a baseline measure.

4. Neoadjuvant therapy
Oncologist, HPB surgeon, radiologist

Pre-treat the patient with chemotherapy, radiation therapy, targeted terapy, immunotherapy or a combination of these to let the tumor tissue shrink in size.

5. Repeat pancreatic imaging protocol
Radiologist, HPB surgeon, oncologist

a. Chest and pelvic CT with contrast.

b. **Consider** MRI, in case of clinically indicated, to investigate indeterminate liver lesions.

c. Imaging report made by radiologist.

Neoadjuvant therapy changes the relevant structures, making it more difficult to distinghuish te tumor.
Difficult to distinguish tumor tissue and scar tissue in CT scan after neoadjuvant therapy.
No fusion of the pre- and post- neoadjuvant treatment CT/MRI.

AI
Determine/segment what is tumor tissue and scar tissue.
Fusion of medical imaging pre- and post- neoadjuvant treatment can help improve the visualization of the effects of neoadjuvant therapy.

6. Blood tests
Pathologist

Test CA 19-9 after biliary drainage, measured after neoadjuvant therapy, to see if the therapy has worked.

Tumor resectable?

No

Yes

Arrow to Phase VIII Systematic treatment

IV. Surgical planning

1. Study the patients anatomical situation
HPB surgeon, vascular surgeon

Investigate the patient specific anatomy and tumor characteristics. Evaluate potential effects of neoadjuvant therapy by comparing the medical imaging with eachother.

Difficulties in visualizing the vascular structures and tumor interactions.
No stereoscopic or depth perception in the currently used imaging.
Planning problems in case of borderline resectable.

3D
Gives a better understanding of the patient specific anatomy.
Visualizes the interactions between vascular structures, tumor tissue and other tissue.
Provide stereoscopic / depth view.
Improves the explanation of the surgical procedure towards the patient and gives a better patient understanding.

2. Determine surgical approach
HPB surgeon, vascular surgeon

a. Open surgery. Can be used for all cases.

b. Laparoscopic surgery. Can be used for the resection of the pancreas tail.

c. Robotic surgery. Can be used for the resection of the pancreas head and taile, and depends on the BMI and the vascularization of the patient.

3. Determine step by step surgical approach
HPB surgeon, vascular surgeon

Decide how to get to the tumor, how to resect it, how to reconstruct everything, where you might get in trouble, etc. Only the difficult parts of the surgery need to be planned.

V. Tumor resection surgery

1. Patient check-in
HPB surgeon (2x), anothesist, OR assistants, vascular surgeon

Relevant intra-operative surgery will be set up.

2. Perform anasthesia
Anothesist, OR assistants

3. Set up and docking of surgical robot (if applicable)
Anothesist, OR assistants

4. Laporascopic inspection
HPB surgeon

a. Inspection to look for metastasis.

b. Discuss possible changed surgical strategy if metastasis or other abnormalities are found.

⚠ Takes valuable time and increase risks of surgery, preferably things like this are determined beforehand so the surgical plan does not have to change.
Surgical team has to make high impact decisions under time pressure during surgery.
Tumor might be unresectable after laparoscopic inspection or even opening up the patient which means you have lost valuable OR time and brought potential risks to the patient.

AI: Improves the decision whether or not the tumor is resectable before the surgery.

3D: 3D and AI can help preventing unexpected situations because of better preparation and visualization of the patient specific situation.

5. Tumor resection
HPB surgeon(s), vascular surgeon, OR assistants

a. Move towards structures of interest and tumor. Evaluate with hands and eyes for potential unexpected abnormalities.

b. Inspect tumor and surrounding tissue and vascularization with frozen sections and US.

c. Resect a lymph node in the pancreas area (if applicable).

d. Recall medical imaging on displays in OR.

e. Carefully resect the abnormality/tumor, part of the pancreas and other relevant structures which need to be resected.

f. Inspect remaining tissue and vascularization for malignant tissue, to confirm whether all malignant tissue is removed.

g. Prepare the resected organs and lymph node for pathologist for further evaluation.

⚠ Moving towards tumor can be difficult, important not to damage artiers, veins, ducts and other surrounding structures.
There are often abnormalities that could not be seen beforehand in the current way of working. This results in changing the surgical plan, taking up extra time.
Sudden help of vascular surgeon might be needed.
Only 2D medical imaging is available in the OR during surgery.
Surgeons have to be extremely careful to make sure they don't cut arteries or veins since the orientation of the vascularization is difficult to understand during surgery.
If the involvement of the tumor in other organs and vessels is underestimated, this might take more time, the surgical plan might have to be adjusted, and perhaps sudden help of a vascular surgeon might be needed. Same for reconstruction.

AI: Improves the decision whether or not the tumor is resectable before the surgery.

3D and AI can help preventing unexpected situations because of better preparation and visualization of the patient specific situation.

3D: Gives a better understanding of the whole situation, making it clearer beforehand whether the help of a vascular surgeon will be needed or not.
Gives extra dimension of feedback on the currently used displays or other visualization techniques during surgery.

6. Reconstruction
HPB surgeon(s), vascular surgeon

a. Reconstruct the digestive system with remaining structures and use stent for the pancreatic duct.

b. Close the patient and end anesthesia.

7. Create surgery report
HPB surgeon

A surgery report is created about all the steps that were taken during the surgery.

8. Patient monitoring after surgery
Nurses

Monitor the patient for complications on the PACU.

VI. Discharge patient

1. Follow-up tests
HPB surgeon, oncologist

Look for signs of cancer return or spread after surgery.

2. Discharge patient
HPB surgeon, oncologist

If recovered from surgery and no further signs of disease progressions are found, the patient can go back home again.

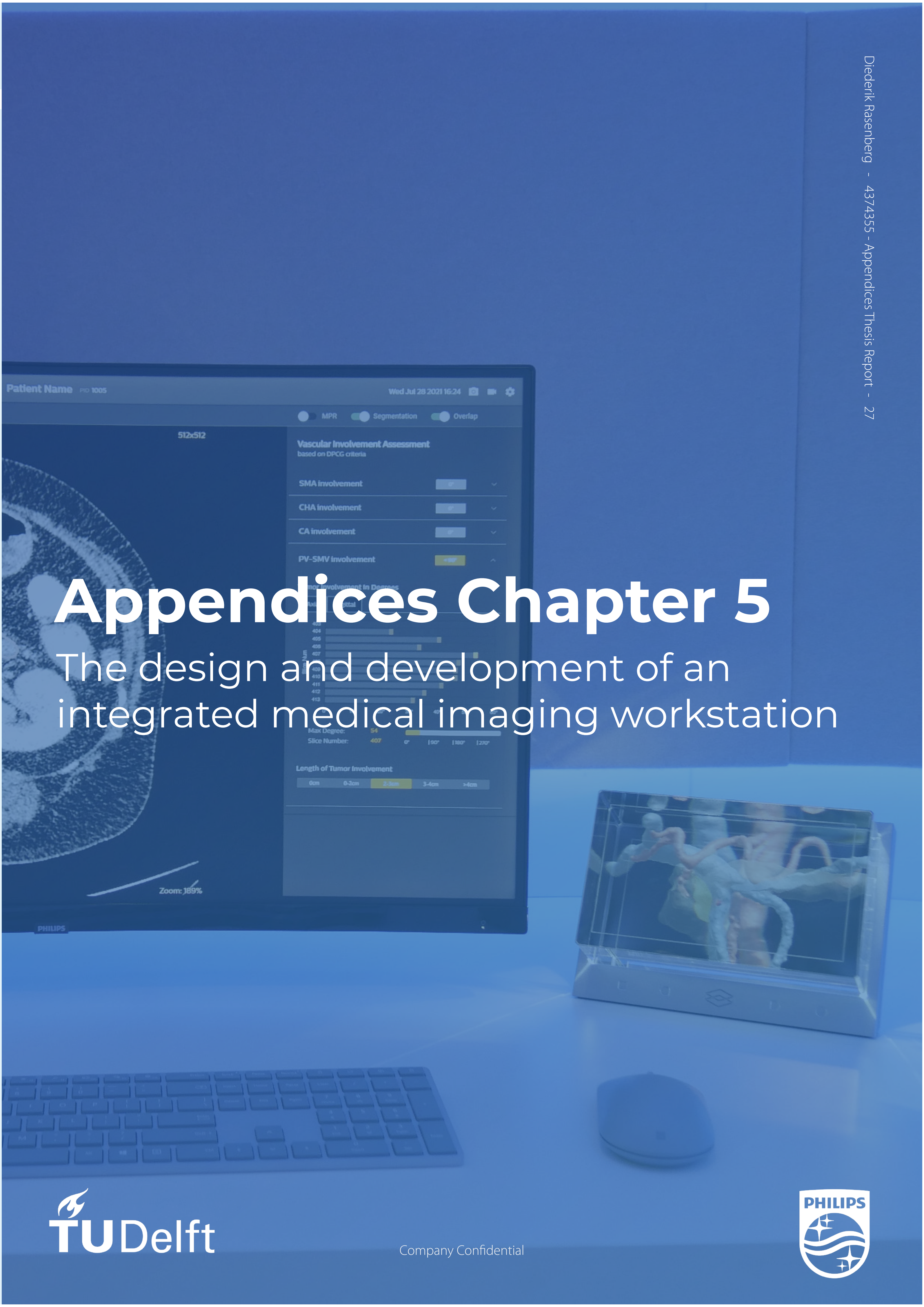
VII. Systemetic treatment

1. Consider adjuvant therapy
HPB surgeon, oncologist, radiologist

Three options for adjuvant therapy: clinical trail (preferred), systematic therapy, systematic therapy followed by chemoradiation.

2. Palliative care
HPB surgeon, oncologist, radiologist

If no treatment options are available anymore, start palliative care to improve the quality of life and extend the lifetime.

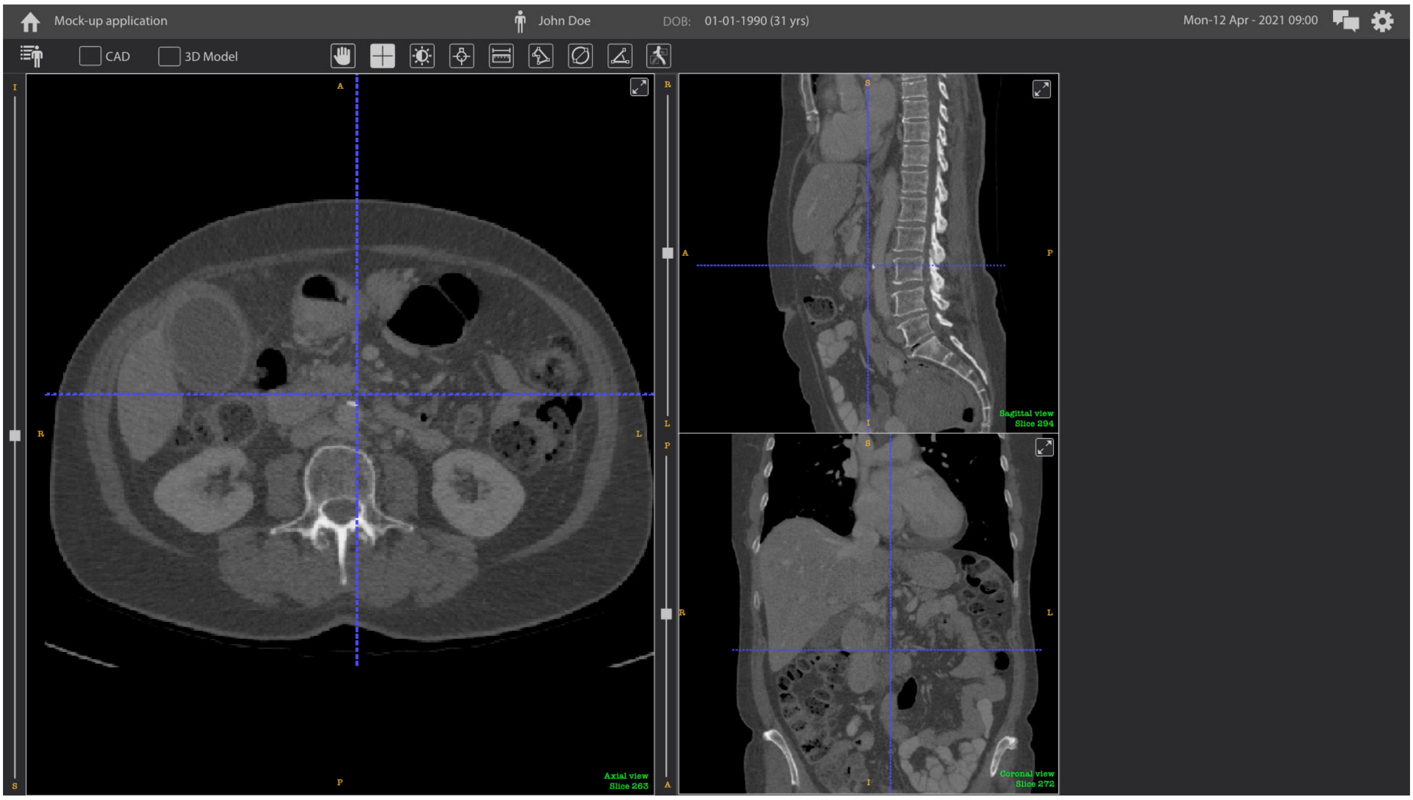


Appendices Chapter 5

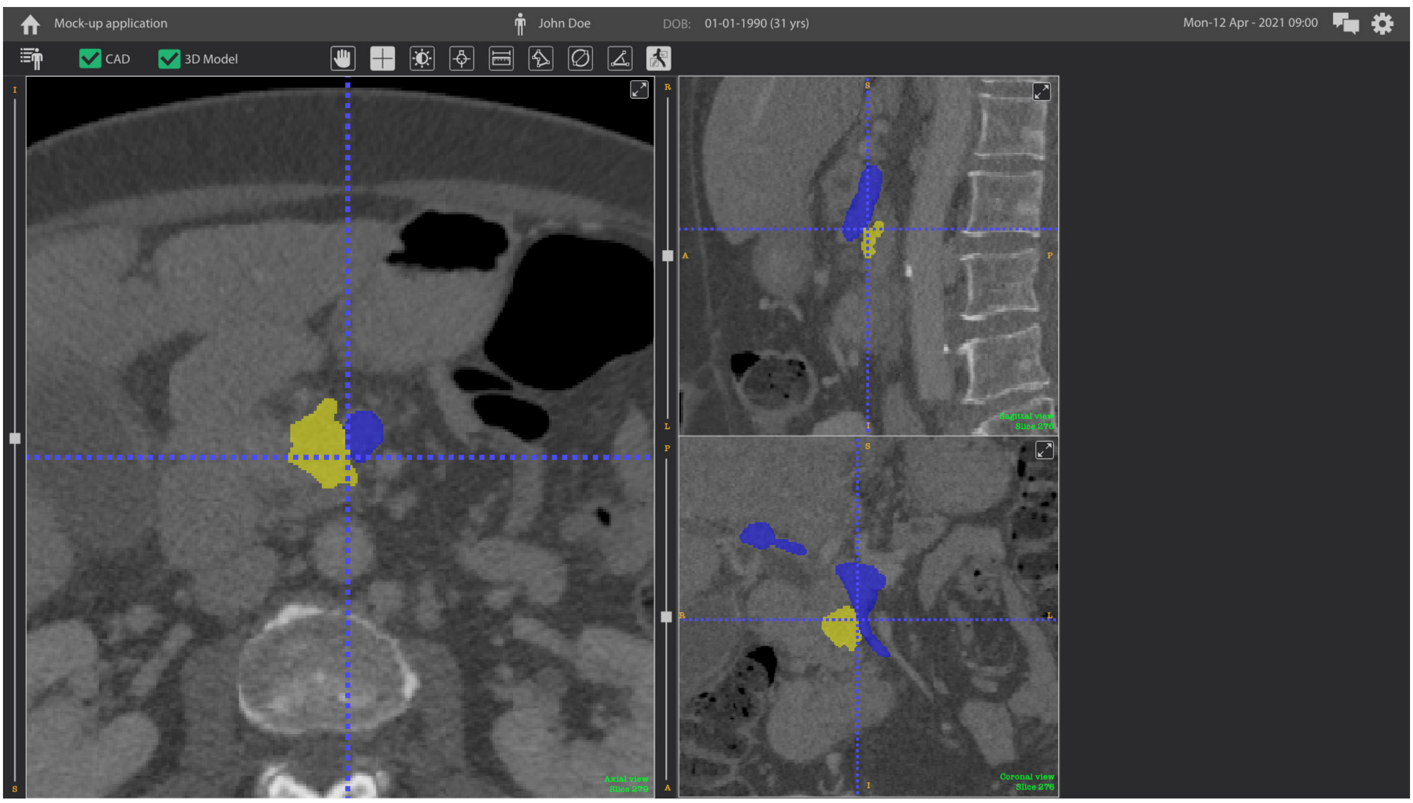
The design and development of an integrated medical imaging workstation

Company Confidential

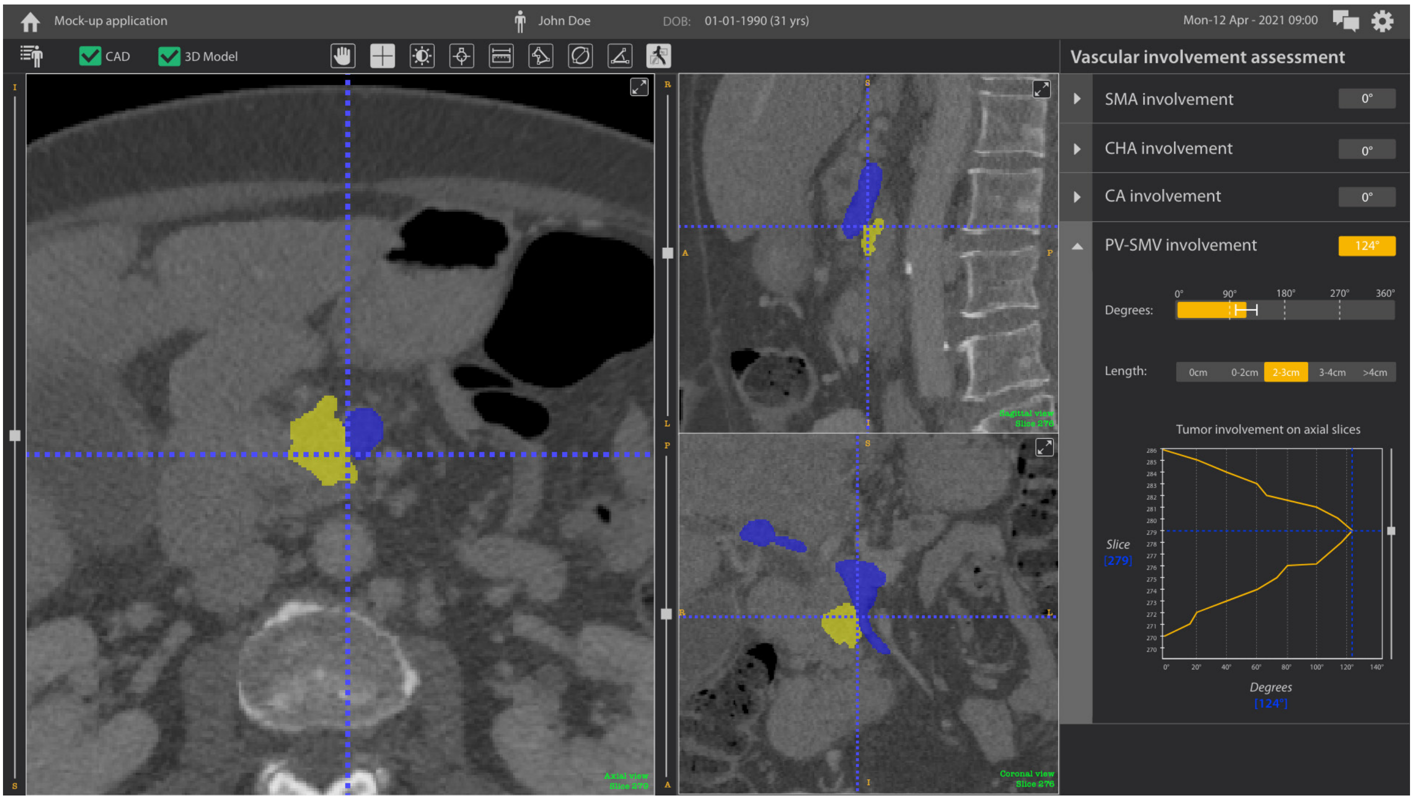
Appendix 5.1 - User-interface design of the medical imaging viewer



Appendix figure 5.1.1. User-interface design of the CT image viewing condition

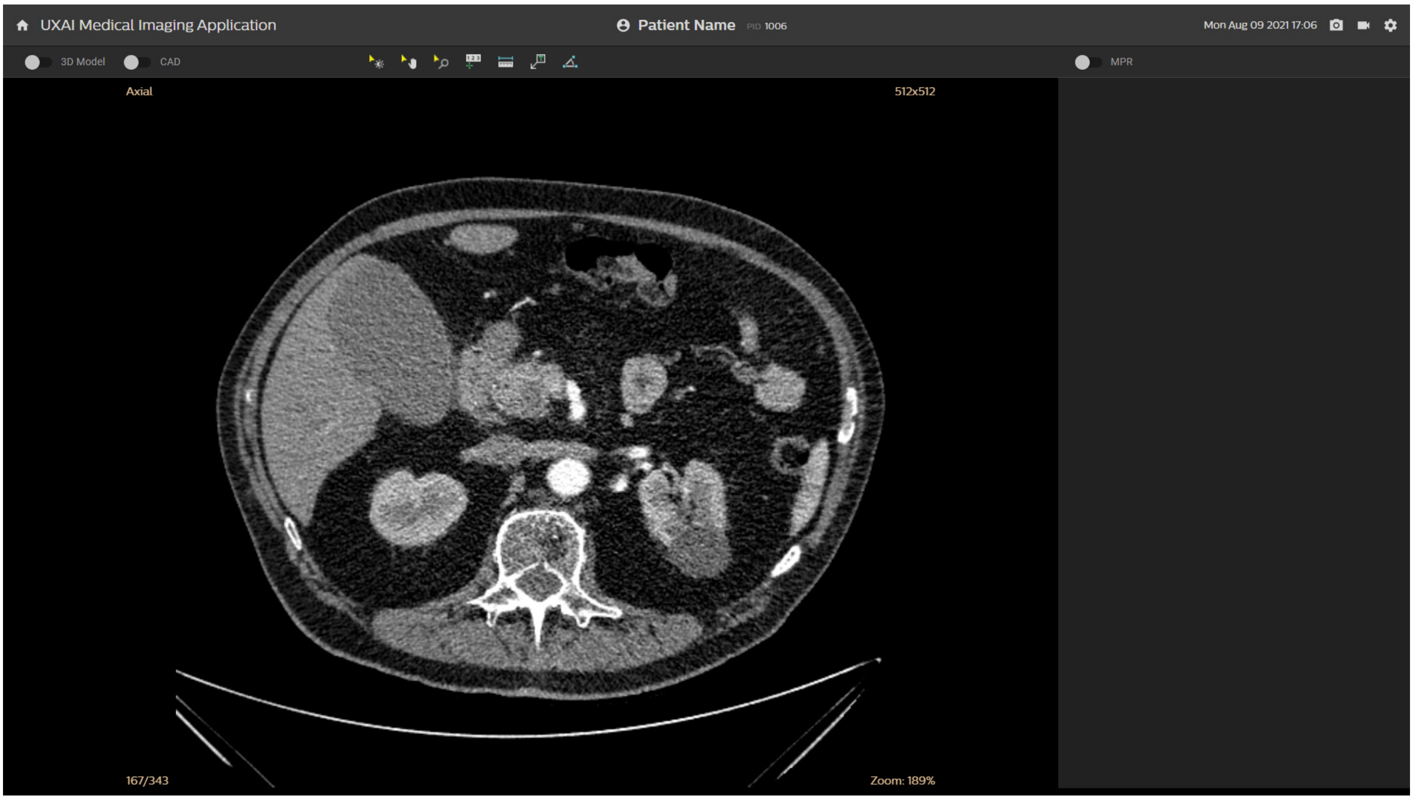


Appendix figure 5.1.2. User-interface design of the 3D image viewing condition. The 3D model would in this condition be displayed on the external 3D display.

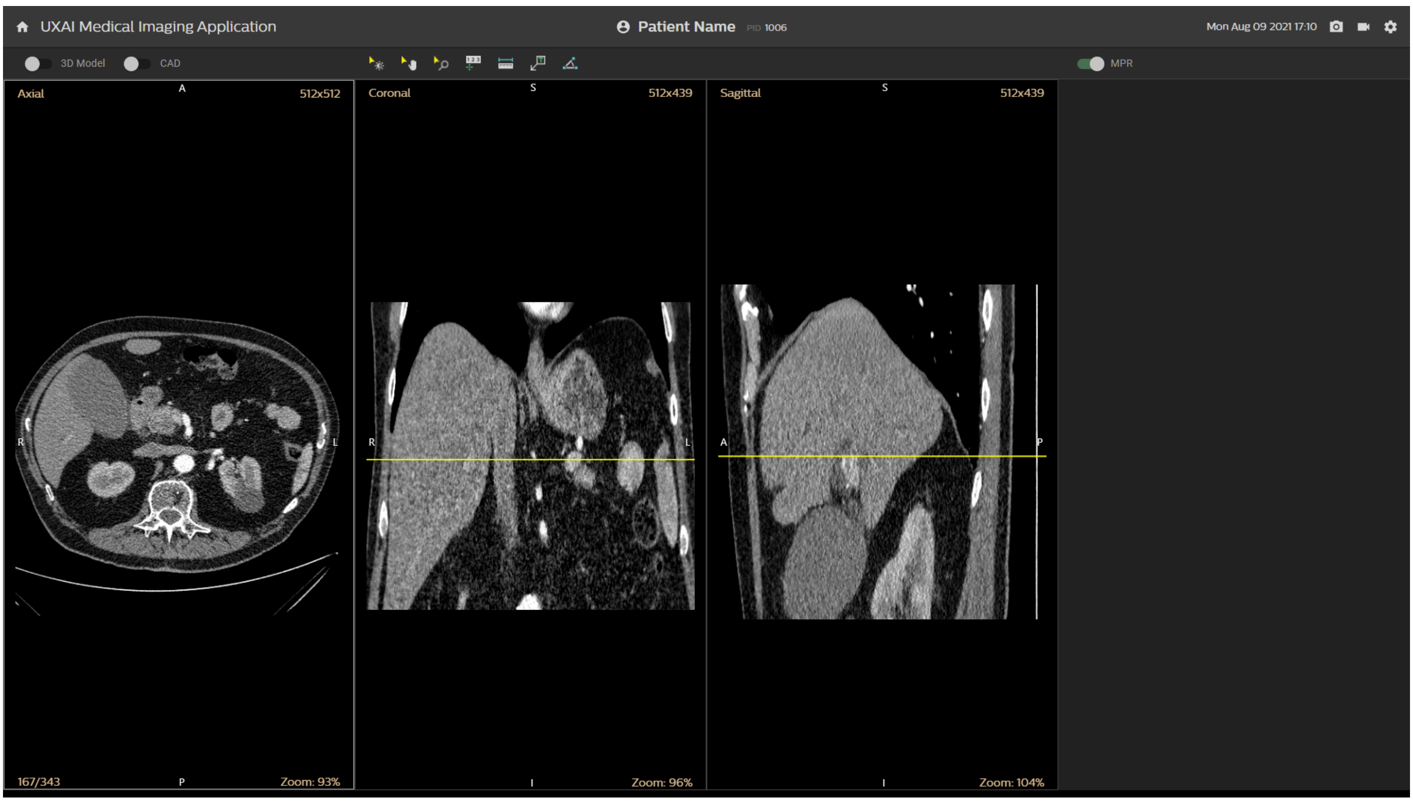


Appendix figure 5.1.3. User-interface design of the CAD image viewing condition. The 3D model would in this condition be displayed on the external 3D display.

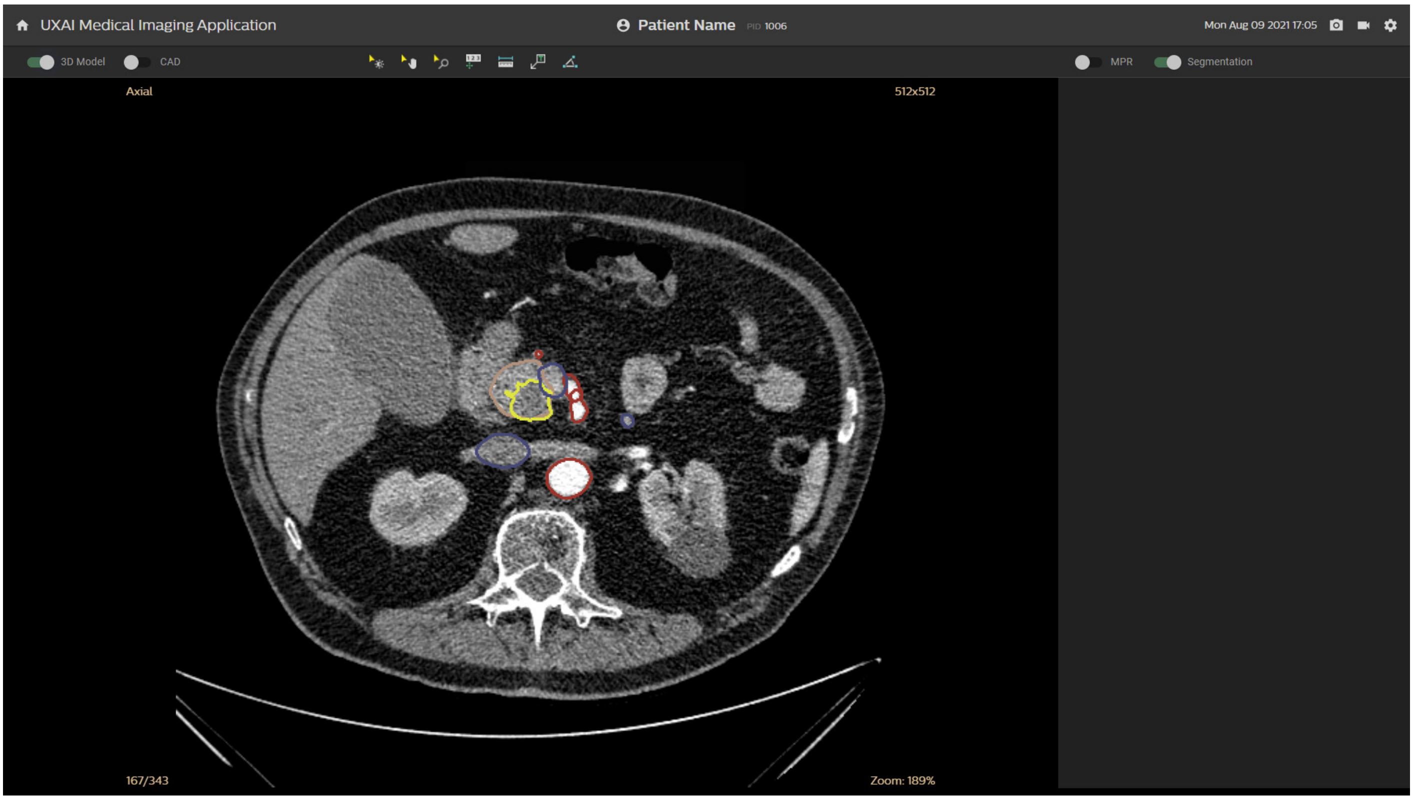
Appendix 5.2 - Screenshots user-interface of working medical imaging viewer



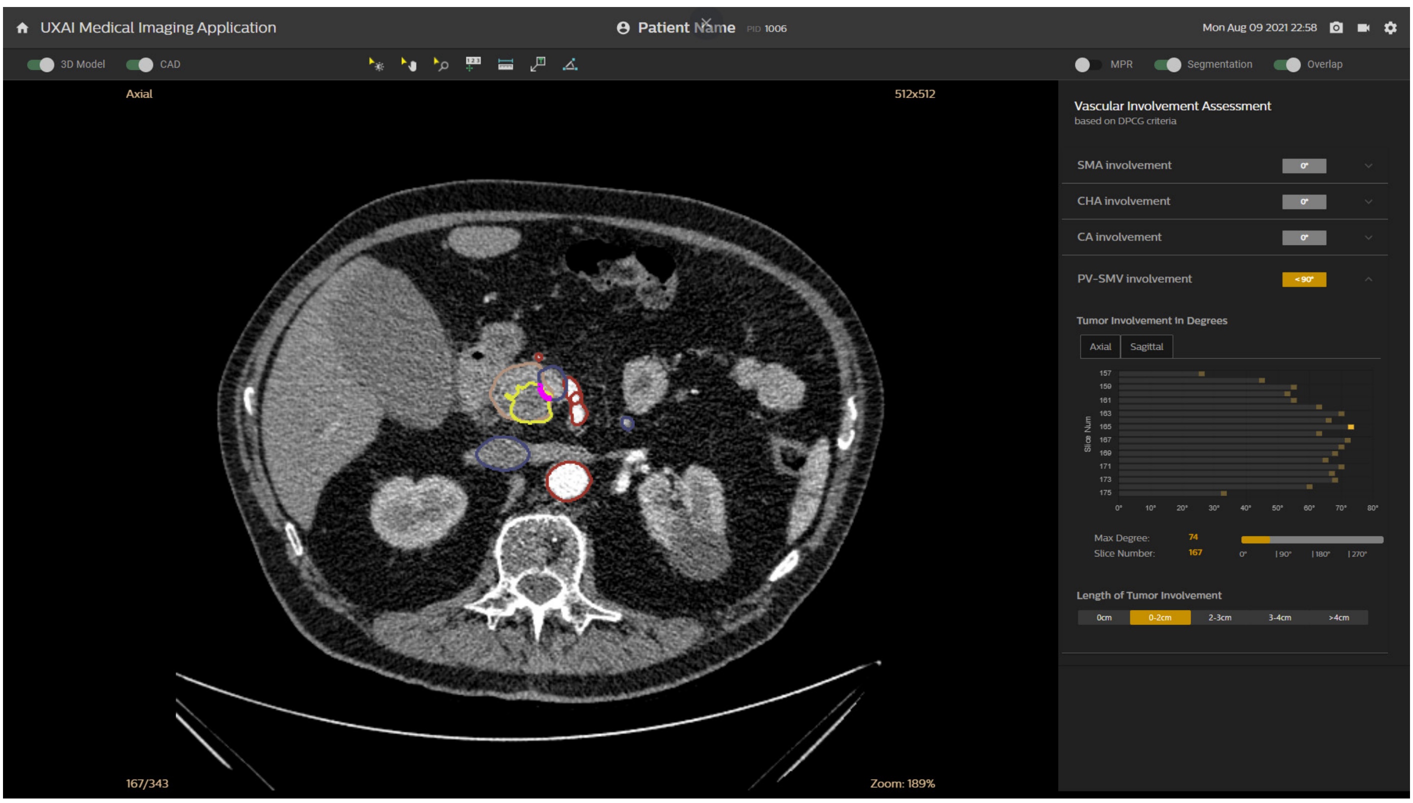
Appendix figure 5.2.1. Screenshot user-interface of the working medical imaging viewer in the CT condition



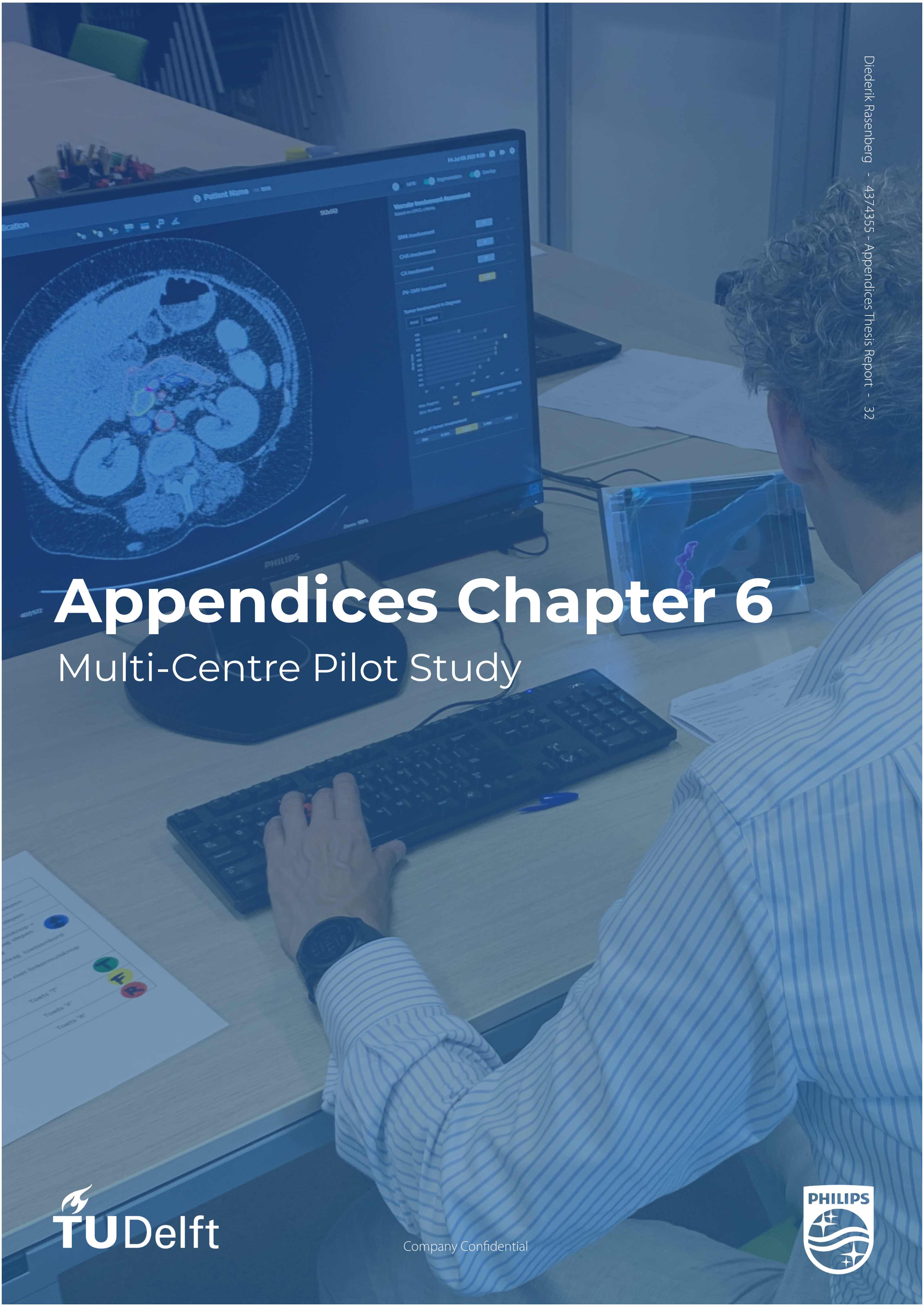
Appendix figure 5.2.1. Screenshot multi-planar reconstruction functionaility (MPR) including reference yellow reference lines of the working medical imaging viewer in the CT condition



Appendix figure 5.2.1. Screenshot user-interface of the working medical imaging viewer in the 3D condition including annotation outlines



Appendix figure 5.2.1. Screenshot user-interface of the working medical imaging viewer in the CAD condition including annotation outlines and the CAD panel showing details regarding vascular involvement



Appendices Chapter 6

Multi-Centre Pilot Study

TU Delft

PHILIPS

Appendix 6.1 - Approval of the Internal Committee for Biomedical Experiments

Approval by the Internal Committee for Biomedical Experiments (ICBE) from Philips for conducting this user-study was required. Accordingly, a study protocol for General Human & Data Studies (excluding Clinical Trials) was developed.

Participants interacted in generative sessions in a simulated setting with the demonstrator (Chapter 5) running on a Philips workstation which was pre-loaded with a set of retrospective and de-identified pancreas cancer cases. The use of retrospective and de-identified pancreas cancer cases received had already been approved in a different study protocol by the ICBE. This study has not influenced any clinical decision making or has any impact on diagnostic workflow of a patient. With respect to COVID-19, materials and people were positioned using a 1.5m social distancing protocol. Participants were able to interact with the demonstrator safely and easily while the study conductors sat at a safe distance observing the participants. Hence, the study objectives could be achieved with implementing necessary risk mitigations with respect to COVID-19. The risk of this study was classified as 'no more than minimal risk'.

Catharina Hospital Eindhoven was in the lead of the recruitment process of participants for this study. Data was acquired in this user-study from the included participants by questionnaires, audio- and video recordings, and written notes. A privacy notice was sent to candidate participants prior participants. This privacy notice provides detailed information on what personal data is collected, why these personal data is collected, with whom the personal data is shared and how long the personal data will be kept. Participants had to read and sign an Information Letter and Informed Consent (ILIC) before participation. The ILIC contained all relevant information regarding why this study is conducted and how it will be conducted. Furthermore, the ILIC contains information regarding the equipment used in the study, involved team members, collection and confidentiality of personal data, COVID-19 measures, their benefits, Philips' confidential information. Participants were able to choose whether they provided permission on collecting photos, screen recording, video recording and audio recording. Additionally, they had to give permission in using those quotes, images, and fragments of the video recordings in external presentations and reports.

Before study protocol approval, it is required that all involved team members that contribute to this study follow mandatory Quality and Regulatory courses from Philips University. The first author was also the study conductor that interacts with study participants and had to follow the following courses: Introduction to ICBE Processes for Research, Introduction to Regulations for Research, Basics in Bioethics: Research Ethics Training for Philips, Introduction to Research Ethics, Good Documentation Practices for Medical Device Manufacturers, Privacy Compliance in Human Studies, and Information Security in Research.

Appendix 6.2 - Baseline patient data

Appendix table 6.2. Baseline patient data received from CZE.

Tumor characteristics	C1 (simple)	C2 (simple)	C3 (simple)	C4 (complex)	C5 (complex)	C6 (complex)
Location	Head	Head	Head	Head	Head	Peri-ampullary
Tumor cross-section (mm)	14	20	23	15	35	30
Density	Hypodense	Isodense	Hypodense	Hypodense	Hyperdense	Hypodense
Dilated pancreatic duct	No	Yes	No	Yes	Yes	No
Dilated common bile duct	Yes	Yes	Yes	No	Yes	Yes
Vascular involvement						
Vascular involvement [RR, SR]	No	No	No	**Yes**	**Yes**	**Yes**
Vessels involved [RR, SR]	None	None	None	**PV-SMV**	**PV-SVM**	**PV-SMV**
Degrees of vascular involvement [RR]	0	0	0	**90°- 180°**	**90° - 180°**	**90° - 180°**
Length of vascular involvement [RR]	0	0	0	N/A	N/A	N/A
Reduction of the vessel lumen [RR]	No	No	No	**<50%**	No	No
Vascular resection [SR]	No	No	No	No	**Yes, interposition graft**	No
Resection margin [PR]	R0	R0	R0	R0	**R1**	R0
Anatomical information						
Anatomical variation [RR, SR]	**Yes**	**Yes**	**Yes**	No	No	**Yes**
Accessibility CA and SMA [RR]	Yes	Yes	Yes	Yes	Yes	Yes
Decision-making						
Resectability [RR]	Resectable	Resectable	Resectable	Resectable	Borderline resectable	Resectable
Surgical technique [SR]	OPD	OPD	OPD	OPD	OPD	OPD

[RR] Extracted from radiology report; [SR] Extracted from surgical report; [PR] Extracted from pathology report. CA = Celiac Axis; SMA = Superior Mesenteric Artery; PV-SMV = Portal Vein – Superior Mesenteric Vein; OPD = Open Pancreaticoduodenectomy.

Appendix 6.3 - Pre-test questionnaire

Participant: ___________________

Part A: General information

1. What is your age?

☐ < 25 years ☐ 26-35 years ☐ 36-45years ☐ 46-55 years ☐ 56-65 years ☐ 66+ years

2. Are you color vision deficient (kleurenblind)?

☐ Yes, type of deficiency _________________________ ☐ No

3. Are you left- or right-handed?

☐ Left ☐ Right

4. What is your medical specialism: _________________________

5. How many years of experience as medical specialist do you have?

☐ < 5 years ☐ 6-10 years ☐ 11-15 years ☐ 16-20 years ☐ >20 years

6. How many open and robot- assisted pancreaticoduodenectomies do you have performed in your carreer?

- Open pancreaticoduodenectomies (OPD): ___________ times
- Robot-assisted pancreaticoduodenectomies (RAPD): ___________ times

7. What imaging modailities do you currently use to evaluate the patient during the preoperative phase of pancreaticoduodenectomies?

...

8a. In the assessment of tumor resectability based on vascular involvement, in what percentage of cases are you NOT confident about the decision?

1	**2**	**3**	**4**	**5**
<20%	<40%	40-60%	>60%	>80%

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8b. Main factors contributing to a lower confidence are:

…

9. In the assessment of pancreatic cancer resectability based on vascular involvement, how frequently do you feel the need for more information?

1 Never	**2** Rarely	**3** Sometimes	**4** Often	**5** Always
Namely:				

10. Among my peers, I am usually the first to try out new information technologies:

1 Strongly disagree	**2** Disagree	**3** Neutral	**4** Agree	**5** Strongly agree

Three-dimensional visualization techniques

11. Do you use or have used 3D stereoscopic displays?

In work / clinical setting

1 Never	**2** Rarely	**3** Sometimes	**4** Often	**5** Always

In personal setting (e.g. in gaming)

1 Never	**2** Rarely	**3** Sometimes	**4** Often	**5** Always

12. Do you use or have used Virtual Reality or Augmented Reality display techniques?

In work / clinical setting

1 Never	**2** Rarely	**3** Sometimes	**4** Often	**5** Always

In personal setting (e.g. in gaming)

1 Never	**2** Rarely	**3** Sometimes	**4** Often	**5** Always

Computer Aided Detection and Diagnosis

13. In your daily clinical work, how frequently do you work with Computer Aided Detection* tools?

1 Never	**2** Rarely	**3** Sometimes	**4** Often	**5** Always

14. How frequently do you trust the output given by Computer Aided Detection* tools?

1 Never	**2** Rarely	**3** Sometimes	**4** Often	**5** Always

15. What is your general opinion about Computer Aided Detection* tools?

…

** Computer Aided Detection tools focus on highlighting, segmenting, or measuring potentially interesting anatomical structures or areas (e.g., nodule detection). Interpretation is done by the radiologist (e.g., tumor is likely malignant).*

16. In your daily clinical work, how frequently do you work with Computer Aided Diagnosis** tools?

1 Never	**2** Rarely	**3** Sometimes	**4** Often	**5** Always

17. How frequently do you trust the output given by Computer Aided Diagnosis** tools?

1 Never	**2** Rarely	**3** Sometimes	**4** Often	**5** Always

18. What is your general opinion about Computer Aided Diagnosis* tools?

…

** Computer Aided Detection tools focus on highlighting, segmenting, or measuring potentially interesting anatomical structures or areas (e.g., nodule detection). Interpretation is done by the radiologist (e.g., tumor is likely malignant).*

Part B: Pre-test questionnaire to measure clinical needs

Philips has explored and identified in collaboration with Catharina Hospital Eindhoven different clinical needs of HPB-surgeons during the preoperative planning of pancreaticoduodenectomies.

In this questionnaire, we want to explore how these identified clinical needs are fulfilled in **current practice** with the **currently available imaging modalities**. If clinical needs of HPB surgeons are missing in this list, you can state these needs at the end of the questionnaire.

If a question is **not applicable**, please do not fill in a score.

Tumor detection and localization

	By means of the currently available medical imaging modailities…	**Strongly disagree**	**Disgree**	**Neither agree nor disagree**	**Agree**	**Strongly agree**
1	I am able to accurately detect/localize pancreatic tumors.	1	2	3	4	5
2	I feel that non-expert hospitals have a sufficient accuracy in detecting/localizing pancreatic tumors and refer patients in time to expert hospitals.	1	2	3	4	5
3	I am able to detect metastases (in liver, lymph node, and other organs).	1	2	3	4	5
Comments:						

Preoperative tumor assessment

	By means of the currently available medical imaging modailities…	**Strongly disagree**	**Disgree**	**Neither agree nor disagree**	**Agree**	**Strongly agree**
4	I am able to discriminate between types of abnormalities (carcinoma, benign tumor, pancreatitis).	1	2	3	4	5
5	I am able to discriminate between tumor, inflammatory and healthy tissue before neoadjuvant therapy.	1	2	3	4	5
6	I am able to discriminate between tumor, inflammatory, fibrotic, treated and healthy tissue after neoadjuvant therapy.	1	2	3	4	5
Comments:						

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Preoperative vascular involvement assessment

	By means of the currently available medical imaging modailities…	Strongly disagree	Disgree	Neither agree nor disagree	Agree	Strongly agree
7	I am able to accurately determine the degrees of contact between the tumor and vascular structures.	1	2	3	4	5
8	I am able to accurately determine the length of the tumor-vessel contact trajectory.	1	2	3	4	5
9	I am able to accurately determine the extend of vascular ingrowth of the tumor in the relevant vessels.	1	2	3	4	5
Comments:						

Preoperative anatomical understanding

	By means of the currently available medical imaging modailities…	Strongly disagree	Disgree	Neither agree nor disagree	Agree	Strongly agree
10	I am able to accurately identify/localize and understand the spatial conformation of the anatomy (e.g. bifurcation of jejunal branch).	1	2	3	4	5
11	I am able to identify/localize potential anatomical variations	1	2	3	4	5
12	I am able to determine if I need I do a vascular resection and how I need to reconstruct the vessel.	1	2	3	4	5
13	I am able to identify (patient specific) anatomical waypoints/landmarks that affirm my surgical approach.	1	2	3	4	5
Comments:						

Preoperative vascular involvement assessment

	By means of the currently available medical imaging modailities…	Strongly disagree	Disgree	Neither agree nor disagree	Agree	Strongly agree
7	I am able to accurately determine the degrees of contact between the tumor and vascular structures.	1	2	3	4	5
8	I am able to accurately determine the length of the tumor-vessel contact trajectory.	1	2	3	4	5
9	I am able to accurately determine the extend of vascular ingrowth of the tumor in the relevant vessels.	1	2	3	4	5
Comments:						

Preoperative anatomical understanding

	By means of the currently available medical imaging modailities…	Strongly disagree	Disgree	Neither agree nor disagree	Agree	Strongly agree
10	I am able to accurately identify/localize and understand the spatial conformation of the anatomy (e.g. bifurcation of jejunal branch).	1	2	3	4	5
11	I am able to identify/localize potential anatomical variations	1	2	3	4	5
12	I am able to determine if I need I do a vascular resection and how I need to reconstruct the vessel.	1	2	3	4	5
13	I am able to identify (patient specific) anatomical waypoints/landmarks that affirm my surgical approach.	1	2	3	4	5
Comments:						

Appendix 6.4 - Case order and participant groups

Appendix table 6.4. Case order and participant groups

Participant group	User-test condition		
	CT-condition	3D-condition	CAD-condition
Group 1 (n=5)	Patient case 1	Patient case 5	Patient case 3
	Patient case 4	Patient case 2	Patient case 6
Group 2 (n=5)	Patient case 3	Patient case 1	Patient case 5
	Patient case 6	Patient case 4	Patient case 2
Group 3 (n=4)	Patient case 5	Patient case 3	Patient case 1
	Patient case 2	Patient case 6	Patient case 4

Appendix 6.5 - Preoperative planning form

PC: **Patient code:** **Group:** **1** (CT) / **2** (3D) / **3** (QUANT)

1) Vascular involvement?	○ No contact ○ Yes, contact ○ Yes, ingrowth ○ Not to be determined
2A) Number of degrees involvement? **2B)** Length of the involved trajectory? **2C)** Reduction of vessel lumen? (Choose: 0% / <50% / >50% / 100%)	**SMA:** ………. degrees ………. mm ………. % **CHA:** ………. degrees ………. mm ………. % **CA:** ………. degrees ………. mm ………. % **PV-SMV:** ………. degrees ………. Mm ………. %
3) Anatomical variant?	○ No, normal ○ Yes, …………………………
4) CA and/or SMA accessible?	○ Yes, both ○ Stenoses CA ○ Not to be determined ○ Stenosis SMA
5A) Resectability (according DPCG criteria)?	○ Resectable ○ Borderline resectable ○ Irresectable
5B) Confidence level resectability (1-10)?	Low … High 1 2 3 4 5 6 7 8 9 10
6A) Neoadjuvant therapy?	○ Yes ○ No
6B) Confidence level neoadjuvant therapy (1-10)?	Low … High 1 2 3 4 5 6 7 8 9 10
7A) Vascular resection needed?	○ Yes ○ No ○ Not to be determined
7B) Confidence level vascular resection (1-10)?	Low … High 1 2 3 4 5 6 7 8 9 10
8A) Surgical technique?	○ OPD ○ RAPD
8B) Confidence level surgical technique (1-10)?	Low … High 1 2 3 4 5 6 7 8 9 10
9) Seen over the course of the complete case; Is there any aspect of the displayed information that makes you more or less confident? If so, what and why?	○ More ○ Less ○ Not applicable What information? Why?
10) Comments?	

Appendix 6.6 - Post-test questionnaire

Prost-test questionnaire to measure clinical needs

We want to explore in this questionnaire how the identified clinical needs are fulfilled (Likert scale) in the situation when your preoperative planning would be supported by means of this prototype.

You have evaluated and assessed two cases of pancreatic cancer per user-test condition, namely the CT-, the 3D- and the Quantifications- (in short CAD) group. For each question it is the intention to score the need fulfillment per user-test condition.

If a question is **not applicable**, please do not fill in a score.

Participant: ______________________

Tumor detection and localization

	With the help of this prototype…		**Strongly disagree**	**Disgree**	**Neither agree nor disagree**	**Agree**	**Strongly agree**
1	I am able to accurately detect/localize pancreatic tumors.	**CT**	1	2	3	4	5
		CT+3D	1	2	3	4	5
		CT+3D+CAD	1	2	3	4	5
2	I feel that non-expert hospitals have a sufficient accuracy in detecting/localizing pancreatic tumors and refer patients in time to expert hospitals.	**CT**	1	2	3	4	5
		CT+3D	1	2	3	4	5
		CT+3D+CAD	1	2	3	4	5
3	I am able to detect metastases (in liver, lymph node, and other organs).	**CT**	1	2	3	4	5
		CT+3D	1	2	3	4	5
		CT+3D+CAD	1	2	3	4	5
Comments:							

Preoperative vascular involvement assessment

	With the help of this prototype…		**Strongly disagree**	**Disgree**	**Neither agree nor disagree**	**Agree**	**Strongly agree**
4	I am able to discriminate between types of abnormalities (carcinoma, benign tumor, pancreatitis).	**CT**	1	2	3	4	5
		CT+3D	1	2	3	4	5
		CT+3D+CAD	1	2	3	4	5
5	I am able to discriminate between tumor, inflammatory and healthy tissue before neoadjuvant therapy.	**CT**	1	2	3	4	5
		CT+3D	1	2	3	4	5
		CT+3D+CAD	1	2	3	4	5

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6	I am able to discriminate between tumor, inflammatory, fibrotic, treated and healthy tissue after neoadjuvant therapy.	CT	1	2	3	4	5
		CT+3D	1	2	3	4	5
		CT+3D+CAD	1	2	3	4	5

Comments:

Preoperative anatomical understanding

	With the help of this prototype…		Strongly disagree	Disgree	Neither agree nor disagree	Agree	Strongly agree
7	I am able to accurately determine the degrees of contact between the tumor and vascular structures.	CT	1	2	3	4	5
		CT+3D	1	2	3	4	5
		CT+3D+CAD	1	2	3	4	5
8	I am able to accurately determine the length of the tumor-vessel contact trajectory.	CT	1	2	3	4	5
		CT+3D	1	2	3	4	5
		CT+3D+CAD	1	2	3	4	5
9	I am able to accurately determine the extend of vascular ingrowth of the tumor in the relevant vessels.	CT	1	2	3	4	5
		CT+3D	1	2	3	4	5
		CT+3D+CAD	1	2	3	4	5

Comments:

Intraoperative anatomical understanding

	With the help of this prototype…		Strongly disagree	Disgree	Neither agree nor disagree	Agree	Strongly agree
10	I am able to accurately identify/localize and understand the spatial conformation of the anatomy (e.g. bifurcation of jejunal branch).	CT	1	2	3	4	5
		CT+3D	1	2	3	4	5
		CT+3D+CAD	1	2	3	4	5
11	I am able to identify/localize potential anatomical variations	CT	1	2	3	4	5
		CT+3D	1	2	3	4	5
		CT+3D+CAD	1	2	3	4	5
12	I am able to determine if I need I do a vascular resection and how I need to reconstruct the vessel.	CT	1	2	3	4	5
		CT+3D	1	2	3	4	5
		CT+3D+CAD	1	2	3	4	5

13	I am able to identify (patient specific) anatomical waypoints/landmarks that affirm my surgical approach.	**CT**	1	2	3	4	5
		CT+3D	1	2	3	4	5
		CT+3D+CAD	1	2	3	4	5
Comments:							

Intraoperative anatomical understanding

	With the help of this prototype…		Strongly disagree	Disgree	Neither agree nor disagree	Agree	Strongly agree
14	I am able to create a common understanding within the surgical team of the patient specific anatomy and the surgical plan.	**CT**	1	2	3	4	5
		CT+3D	1	2	3	4	5
		CT+3D+CAD	1	2	3	4	5
15	I have a good view of the tumor and the surrounding anatomical structures during open surgery.	**CT**	1	2	3	4	5
		CT+3D	1	2	3	4	5
		CT+3D+CAD	1	2	3	4	5
16	I have a good view of the tumor and the surrounding anatomical structures during minimally invasive (robot) surgery.	**CT**	1	2	3	4	5
		CT+3D	1	2	3	4	5
		CT+3D+CAD	1	2	3	4	5
Comments:							

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CAD evaluation

To answer the questions in this section, the participants must take only the quantifications group into consideration.

1. In exploring and assessing the two pancreatic cases in the quantifications group, how frequently did you understand why* the CAD provided these suggestions?

** e.g., what it based the recommendations on, how it interpreted the findings, etc.*

1 Never	**2** Rarely	**3** Sometimes	**4** Often	**5** Always
Why (not)?				
What do you think can help you to better understand why the CAD provided these recommendations?				

2. In exploring and assessing the two pancreatic cases in the quantifications group, how frequently did you trust the recommendations given by the CAD?

1 Never	**2** Rarely	**3** Sometimes	**4** Often	**5** Always
Why (not)?				
What do you think can help you to better trust the CAD recommendations?				

3. In exploring and assessing the two pancreatic cases in the quantifications group, how frequently was there any conflict between your judgement and the CAD recommendation?

1 Never	**2** Rarely	**3** Sometimes	**4** Often	**5** Always
If so, how did you think and feel about this conflict?				

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Why (not)?

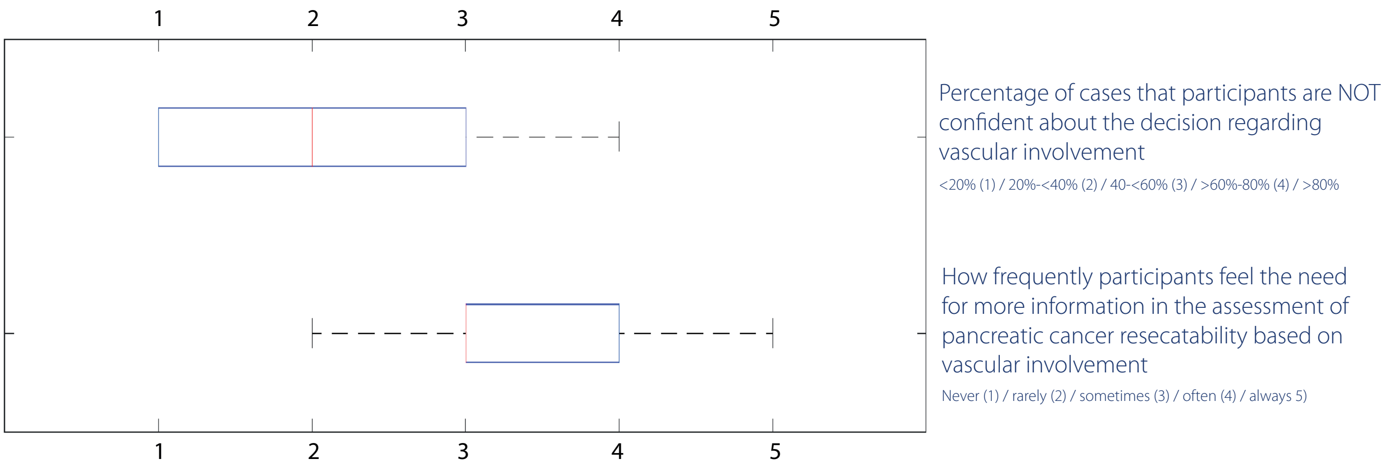
4. In exploring and assessing the two pancreatic cases in the quantifications group, how frequently did the CAD change your mind about the conclusion?

1 Yes	**2** No
If yes, how is it different?	
If yes, what caused this change?	

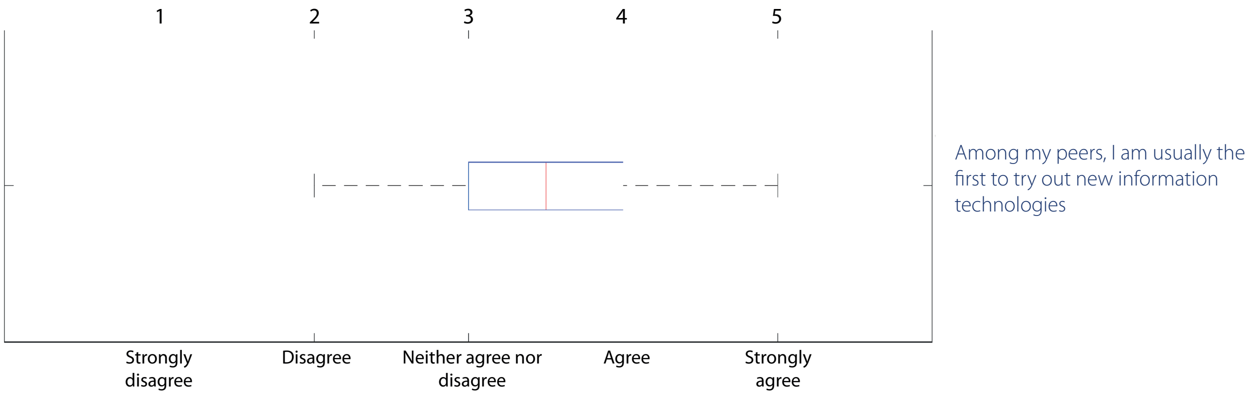
5. After having explored and assessed the two pancreatic cases in the quantifications group, did your general opinion on CAD change?

1 Yes	**2** No
If yes, how is it different?	
If yes, what caused this change?	
If yes, how did this changed our opinion on future CAD-suggestion(s)?	

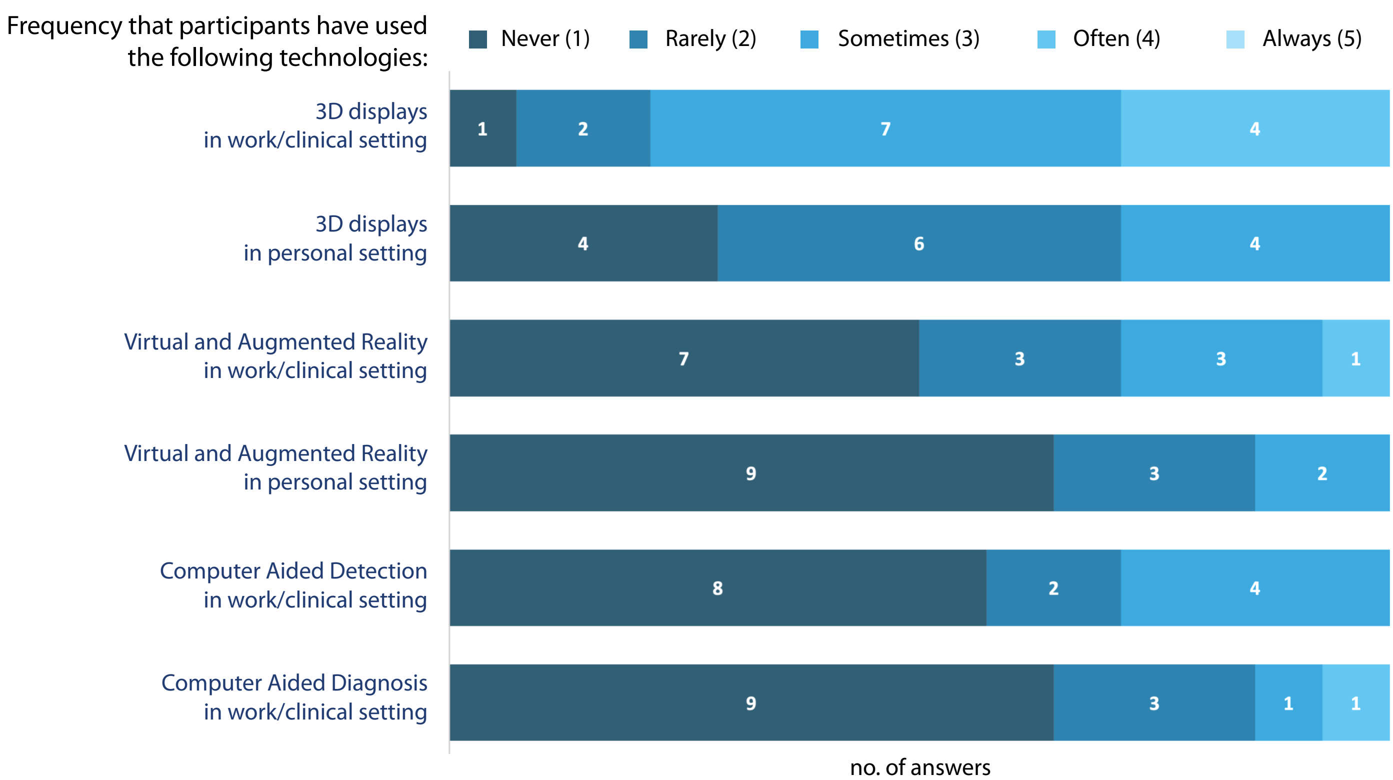
Appendix 6.7 - Box plots regarding experience participants



Appendix figure 6.7.1. Box plots of showing the uncertainty and need for more information in vascular involvement assessment



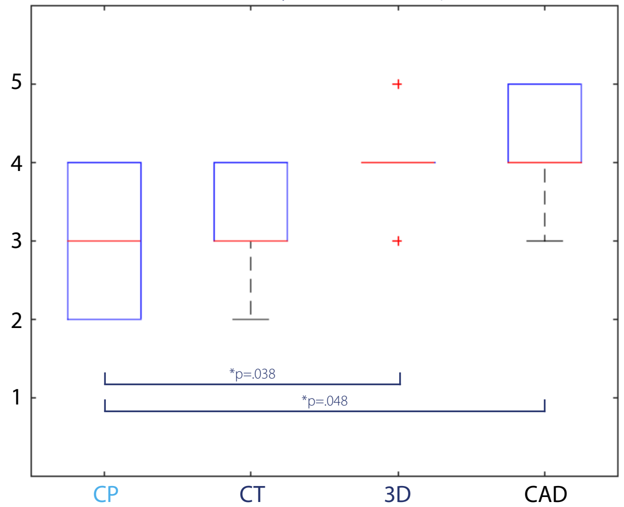
Appendix figure 6.7.2. Box plot of the tech savviness of included participants.



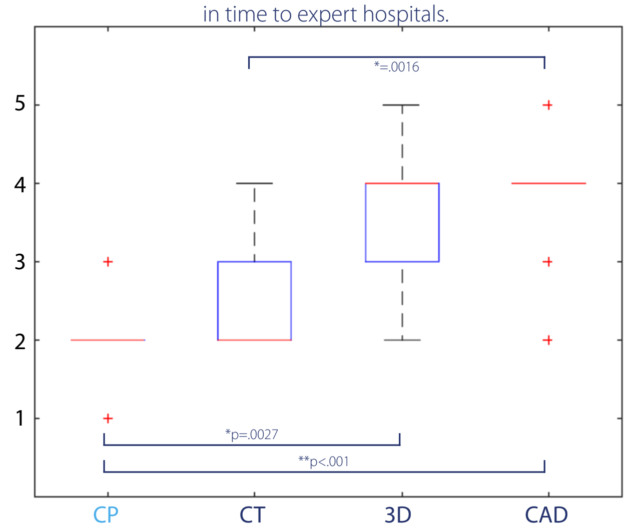
Appendix figure 6.7.3 Stacked bar charts regarding experience of participants with 3D visualization and CAD technologies (Likert scale).

Appendix 6.8 - Perceived fulfilment of clinical needs

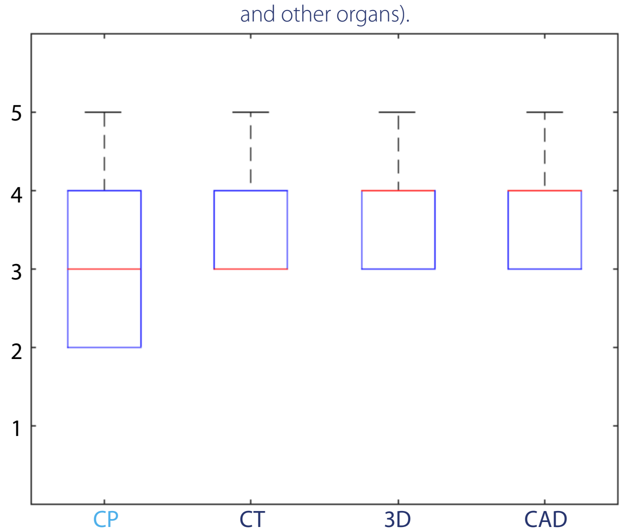
N1 - I am able to accurately detect/localize pancreatic tumors.



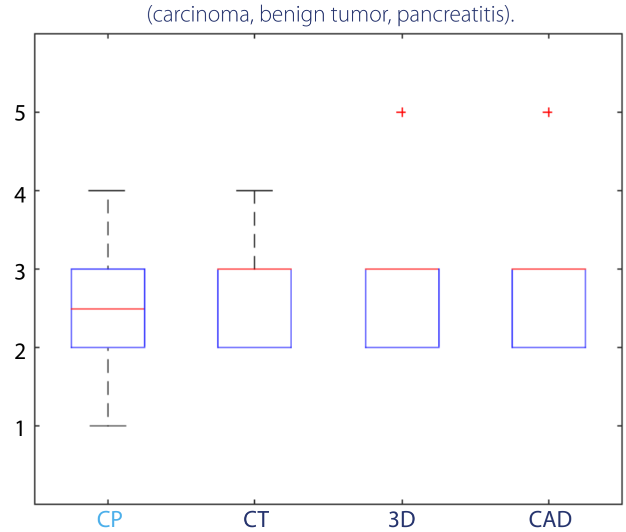
N2 - I feel that non-expert hospitals have a sufficient accuracy in detecting/localizing pancreatic tumors and refer patients in time to expert hospitals.



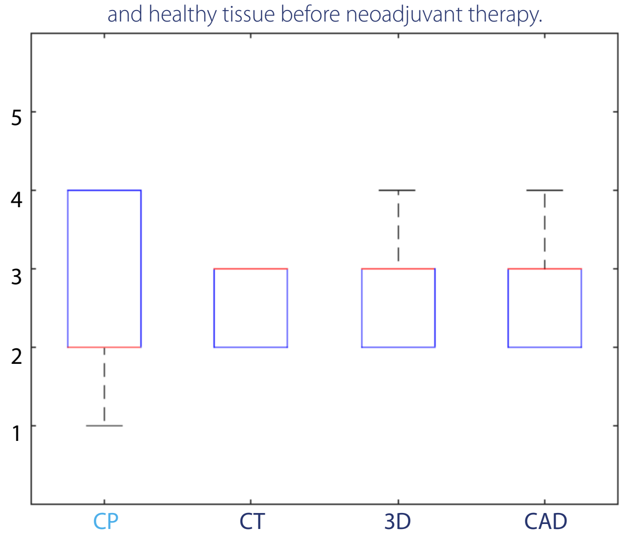
N3 - I am able to detect metastases (in liver, lymph node, and other organs).



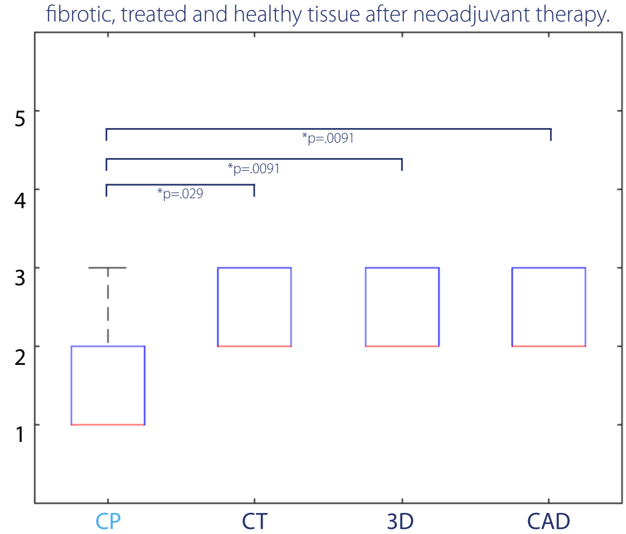
N4 - I am able to discriminate between types of abnormalities (carcinoma, benign tumor, pancreatitis).



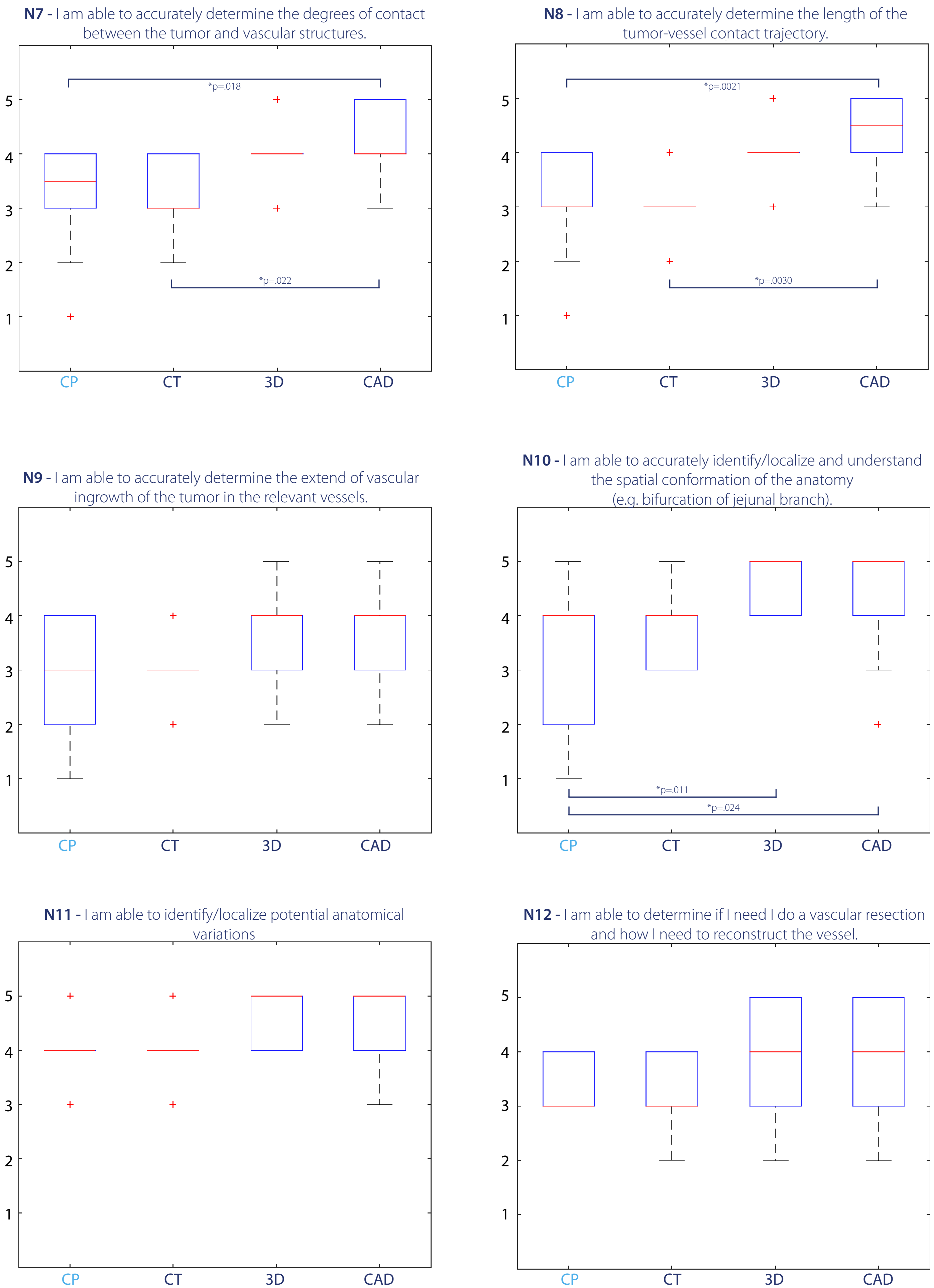
N5 - I am able to discriminate between tumor, inflammatory and healthy tissue before neoadjuvant therapy.



N6 - I am able to discriminate between tumor, inflammatory, fibrotic, treated and healthy tissue after neoadjuvant therapy.

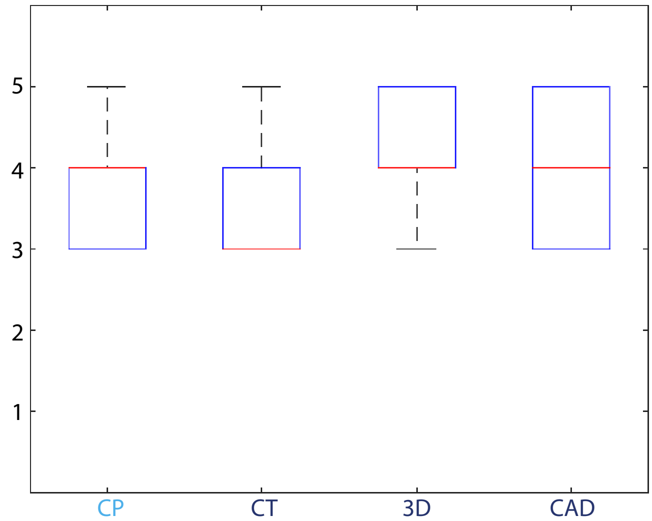


Appendix figure 6.8.1. Box plots regarding perceived fulfilment of clinical needs (Likert scale); CP = current practice (pre-test); CT = computed tomography group; 3D = 3D group; CAD = Quantifications group. Red lines = medians; blue boxes = 25th and 75th percentile; red crosses = outlier values; dotted black line = range of values. *p < .05; **p<.001.

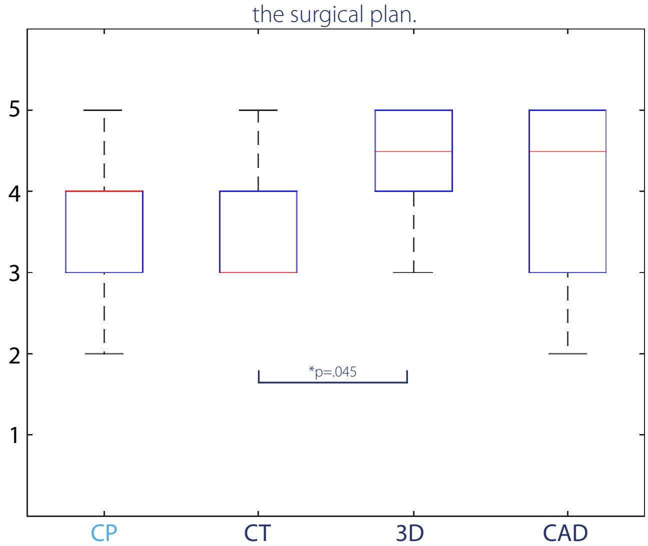


Appendix figure 6.8.2 Box plots regarding perceived fulfilment of clinical needs (Likert scale); CP = current practice (pre-test); CT = computed tomography group; 3D = 3D group; CAD = Quantifications group. Red lines = medians; blue boxes = 25th and 75th percentile; red crosses = outlier values; dotted black line = range of values. *p < .05; **p<.001.

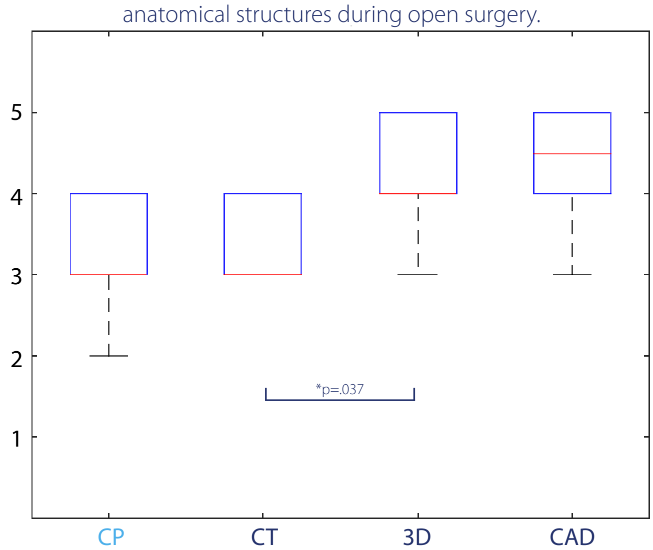
N13 - I am able to identify (patient specific) anatomical way-points/landmarks that affirm my surgical approach.



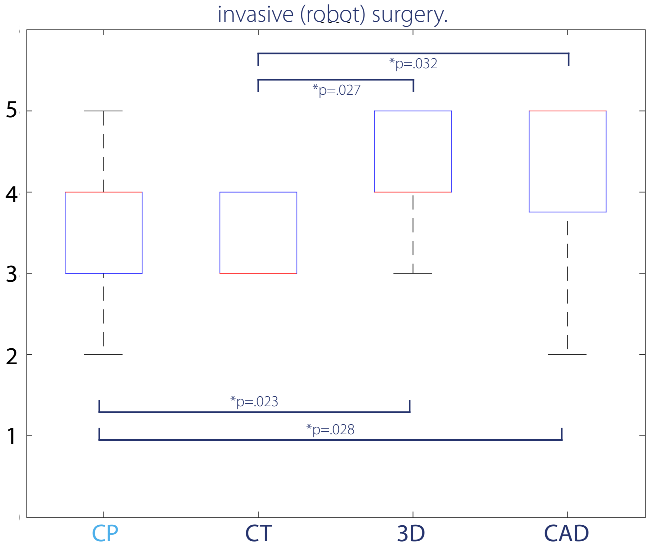
N14 - I am able to create a common understanding within the surgical team of the patient specific anatomy and the surgical plan.



N15 - I have a good view of the tumor and the surrounding anatomical structures during open surgery.



N16 - I have a good view of the tumor and the surrounding anatomical structures during minimally invasive (robot) surgery.



Appendix figure 6.8.3. Box plots regarding perceived fulfilment of clinical needs (Likert scale); CP = current practice (pre-test); CT = computed tomography group; 3D = 3D group; CAD = Quantifications group. Red lines = medians; blue boxes = 25th and 75th percentile; red crosses = outlier values; dotted black line = range of values. *p < .05; **p<.001.

Appendix 6.9 - Preidciton accuracy simulated planning

Appendix Table 6.9.1. Prediction accuracy of vascular involvement part I

Category		Baseline data	CT-condition			3D-condition			CAD-condition		
Vascular Involvement			correct (n)	total (n)	Prediction accuracy (%)	correct (n)	total (n)	Prediction accuracy (%)	correct (n)	total (n)	Prediction accuracy (%)
Type of involvement	All cases combined		24	27	89%	28	28	100%	29	29	100%
	Simple cases		12	13	92%	15	15	100%	14	14	100%
	No involvement	x	12	13		15	15		14	14	
	Venous involvement		1	13							
	Complex cases		12	14	86%	13	13	100%	15	15	100%
	No involvement		1	14							
	Arterial involvement		4	14							
	Venous involvement	x	12	14		13	13		15	15	
Number of degrees	All cases combined		17	27	63%	21	28	75%	21	29	72%
	Simple cases		12	13	92%	15	15	100%	14	14	100%
	C1	0°	4	4	100%	6	6	100%	4	4	100%
	No contact (0°)	x	4	4		6	6		4	4	
	C2	0°	4	4	100%	5	5	100%	5	5	100%
	No contact (0°	x	4	4		5	5		5	5	
	C3	0°	4	5	80%	4	4	100%	5	5	100%
	No contact (0°)	x	4	5		4	4		5	5	
	<90° - PV-SMV		1	5							
	Complex cases		5	14	36%	6	13	46%	7	15	47%
	Complex cases vs CAD outcome		6	14	43%	5	13	38%	11	15	73%
	C4	<90° - PV-SMV	0	5	0%	2	5	40%	2	4	50%
	C4 vs CAD outcome	<90° - PV-SMV	4	5	80%	2	5	40%	2	4	50%
	<90° - PV-SMV	x / CAD				2	5		2	4	
	90°-180° - PV-SMV		4	5		3	5		2	4	
	>180° - PV-SMV		1	5							
	C5	>180° - PV-SMV	3	4	75%	2	4	50%	1	6	17%
	C5 vs CAD outcome	<90° - PV-SMV	1	4	25%	1	4	25%	5	6	83%
	<90° - SMA		1	4							
	<90° - PV-SMV	CAD	1	4		1	4		5	6	
	90°-180° - PV-SMV	x	3	4		2	4		1	6	
	> 180°	x									
	Cannot determine PVSMV contact					1					
	C6	<90° - PV-SMV	2	5	40%	2	4	50%	4	5	80%
	C6 vs CAD outcome	<90° - PV-SMV	1	5	20%	2	4	50%	4	5	80%
	No contact		1	5							
	<90° - PV-SMV	x (CAD)	1	5		2	4		4	5	
	90°-180° - CHA		3	5							
	90°-180° - PV-SMV		2	5		2	4		1	5	
	Cannot determine PVSMV degrees		1	5							

Prediction accuracy was calculated by the formula: (number of correct predictions) / (total number of predictions) x 100%; Correct (n) = correct predictions; Total (n) = total number of predictions. SMA = superior mesenteric artery; CHA = common hepatic artery; PV-SMV = portal vein - superior mesenteric vein; N/A = not available.

Appendix Table 6.9.2. Prediction accuracy of vascular involvement part II

Category		Baseline data	CT-condition			3D-condition			CAD-condition		
Vascular Involvement			correct (n)	total (n)	Prediction accuracy (%)	correct (n)	total (n)	Prediction accuracy (%)	correct (n)	total (n)	Prediction accuracy (%)
Length of trajectory	All cases combined		12	13	92%	15	15	100%	14	14	100%
	Simple cases		12	13	92%	15	15	100%	14	14	100%
	C1	0 mm	4	4	100%	6	6	100%	4	4	100%
	No contact (0 mm)	x	4	4		6	6		4	4	
	C2	0 mm	4	4	100%	5	5	100%	5	5	100%
	No contact (0 mm)	x	4	4		5	5		5	5	
	C3	0 mm	4	5	80%	4	4	100%	5	5	100%
	No contact (0 mm)	x	4	5		4	4		5	5	
	11-20 mm - PV-SMV		1	5							
	Complex cases										
	C4	N/A									
	1-10 mm - PV-SMV					4	5		2	4	
	11-20 mm - PV-SMV		5	5		1	5		2	4	
	21 - 30 mm - PV-SMV										
	C5	N/A									
	1-10 mm - PV-SMV								1	6	
	11-20 mm - PV-SMV		3	4		3	4		2	6	
	21 - 30 mm - PV-SMV								3	6	
	31 - 40 mm - SMA		1	4							
	31 - 40 mm - PV-SMV		1	4							
	Cannot determine PV-SMV length					1	4				
	C6	N/A									
	1-10 mm - CHA		1	5							
	1-10 mm - PV-SMV		3	5		1	4		2	5	
	11-20 mm - PV-SMV					3	4		2	5	
	21 - 30 mm - PV-SMV										
	Cannot determine PV-SMV length		2	5					1	5	
Reduction vessel lumen	All cases combined		20	27	74%	24	28	86%	23	29	79%
	Simple cases	0%	12	13	92%	15	15	100%	14	14	100%
	C1	0%	4	4	100%	6	6	100%	4	4	100%
	No reduction	x	4	4		6	6		4		
	C2	0%	4	4	100%	5	5	100%	5	5	100%
	No reduction	x	4	4		5	5		5		
	C3	0%	4	5	80%	4	4	100%	5	5	100%
	No reduction	x	4	5		4	4		5		
	<50% reduction - PV-SMV		1	5							
	Complex cases		8	14	57%	9	13	69%	9	15	60%
	C4	<50%	1	5	20%	3	5	60%	1	4	25%
	0%		4	5		2	5		3	4	
	<50% - PV-SMV	x	1	5	20%	3	5		1	4	
	C5	0%	3	4	75%	3	4	75%	4	6	67%
	0%	x	3	4		3	4		4	6	
	<50% - PV-SMV		1	4					2	6	
	Cannot determine occlusion - PV-SMV					1	4				
	C6	0%	4	5	80%	3	4	75%	4	5	80%
	0%	x	4	5		3	4		4	5	
	<50% - PV-SMV					1	4		1	5	
	Cannot determine occlusion - PV-SMV		1								

Prediction accuracy was calculated by the formula: (number of correct predictions) / (total number of predictions) x 100%; Correct (n) = correct predictions; Total (n) = total number of predictions. SMA = superior mesenteric artery; CHA = common hepatic artery; PV-SMV = portal vein - superior mesenteric vein; N/A = not available.

Appendix Table 6.9.3. Prediction of accuracy of anatomical assesment

Category		Baseline data	CT-condition			3D-condition			CAD-condition		
Anatomical assessment			correct (n)	Total (n)	Prediction accuracy (%)	correct (n)	total (n)	Prediction accuracy (%)	correct (n)	total (n)	Prediction accuracy (%)
Anatomical variations	All cases combined		22	27	81%	25	28	89%	26	29	90%
	Variation	Yes	14	18	78%	17	19	89%	16	19	84%
	C1	Yes	4	4	100%	5	6	83%	3	4	75%
	C2	Yes	3	4	75%	4	5	80%	4	5	80%
	C3	Yes	4	5	80%	4	4	100%	5	5	100%
	C6	Yes	3	5	60%	4	4	100%	4	5	80%
	No variation	No	8	9	89%	8	9	89%	10	10	100%
	C4	No	5	5	100%	5	5	100%	4	4	100%
	C5	No	3	4	75%	3	4	75%	6	6	100%
SMA and CA accessible	All cases combined		15	27	56%	19	28	68%	18	29	62%
	Simple cases	Yes, both	7	13	54%	10	15	67%	8	14	57%
	C1	Yes, both	4	4	100%	5	6	83%	2	4	50%
	Yes both accessible	x	2	4		5	6		2	4	
	Stenosis CA		2	4		1	6		1	4	
	Cannot determine					1			1	4	
	C2	Yes, both	4	4	100%	4	5	80%	4	5	80%
	Yes both accessible	x	4	4		4	5		4	5	
	Stenosis CA								1	5	
	Cannot determine					1	5				
	C3	Yes, both	1	5	20%	1	4	25%	2	5	40%
	Yes both accessible	x	1	5		1	4		2	5	
	Stenosis CA		2	5		1	4		2	5	
	Stenosis SMA					1	4				
	Stenosis CA and SMA		1	5					1	5	
	Cannot determine		1	5		1	4				
	Complex cases	Yes, both	8	14	57%	9	13	69%	10	15	67%
	C4	Yes, both	2	5	40%	2	5	40%	1	4	25%
	Yes both accessible	x	3	5		3	5		2	4	
	Stenosis CA		2	5		2	5		1	4	
	Cannot determine								1	4	
	C5	Yes, both	2	4	50%	4	4	100%	4	6	67%
	Yes both accessible	x	2	4		4	4		4	6	
	Stenosis CA		1	4					1	6	
	Cannot determine		1	4		1	4		1	6	
	C6	Yes, both	4	5	80%	3	4	75%	5	5	100%
	Yes both accessible	x	4	5		3	4		5	5	
	Stenosis CA		1	5		1	4				

Prediction accuracy was calculated by the formula: (number of correct predictions) / (total number of predictions) x 100%; Correct (n) = correct predictions; Total (n) = total number of predictions. SMA = superior mesenteric artery; CA = celiac axis; N/A = not available.

Appendix Table 6.9.4. Prediction of accuracy of decision-making

Category		Baseline data	CT-condition			3D-condition			CAD-condition		
Decision-making			correct (n)	total (n)	Prediction accuracy (%)	correct (n)	total (n)	Prediction accuracy (%)	correct (n)	total (n)	Prediction accuracy (%)
Resectability	All cases combined		18	27	67%	22	28	79%	22	29	76%
	Simple cases		13	13	100%	15	15	100%	14	14	100%
	C1	Resectable	4	4	100%	6	6	100%	4	4	100%
	C2	Resectable	4	4	100%	5	5	100%	5	5	100%
	C3	Resectable	5	5	100%	4	4	100%	5	5	100%
	Complex cases		5	14	36%	7	13	54%	8	15	53%
	C4	Resectable	1	5	20%	3	5	60%	2	4	50%
	Resectable	x	1	5		3	5		2	4	
	Borderline Resectable		4	5		2	5		2	4	
	C5	Borderline resectable	3	4	75%	2	4	50%	4	6	67%
	Resectable		1	4		2	4		2	6	
	Borderline Resectable	x	3	4		2	4		4	6	
	C6	Resectable	1	5	20%	2	4	50%	2	5	40%
	Resectable	x	1	5		2	4		2	5	
	Borderline Resectable		2	5		2	4		3	5	
	Irresectable		2	5							
Vascular resection	All cases combined		19	27	70%	19	28	68%	18	29	62%
	Simple cases		12	13	92%	14	15	93%	13	14	93%
	C1	No	4	4	100%	6	6	100%	4	4	100%
	C2	No	4	4	100%	4	5	80%	4	5	80%
	No	x	4	4		4	5		4	5	
	Cannot determine					1	5		1	5	
	C3	No	4	5	80%	4	4	100%	5	5	100%
	Yes	x	4	5		4	4		5	5	
	No		1	5							
	Complex cases		7	14	50%	5	13	38%	5	15	33%
	C4	No	2	5	40%	2	5	40%	0	4	0%
	Yes		1	5		3	5		3	4	
	No	x	2	5		2	5				
	Cannot determine		2	5	40%				1	4	
	C5	Yes	2	4	50%	2	4	50%	4	6	67%
	Yes	x	2	4		2	4		4	6	
	No										
	Cannot determine		2	4		2	4		2	6	
	C6	No	3	5	60%	1	4	25%	1	5	20%
	Yes					3	4		4	5	
	No	x	3	5		1	4		1	5	
	Cannot determine		2	5							
Surgical technique	All cases combined		18	27	67%	20	28	71%	16	29	55%
	Simple cases		5	13	38%	10	15	67%	3	14	21%
	C1	OPD	2	4	50%	6	6	100%	1	4	25%
	OPD	x	2	4		6	6		1	4	
	RAPD		3	4					4	4	
	C2	OPD	2	4	50%	3	5	60%	1	5	20%
	OPD	x	2	4		3	5		1	5	
	RAPD		2	4		3	5		4	5	
	C3	OPD	1	5		1	4	25%	1	5	20%
	OPD	x	1	5		1	4		1	5	
	RAPD		4	5		3	4		4	5	
	Complex cases		13	14	93%	10	13	77%	13	15	87%
	C4	OPD	5	5	100%	2	5	40%	4	4	100%
	OPD	x	5	5		2	5		4	4	
	RAPD		1	5		3	5				
	C5	OPD	4	4	100%	4	4	100%	5	6	83%
	OPD	x	4	4		4	4		5	6	
	RAPD								1	6	
	C6	OPD	4	5	80%	4	4	100%	4	5	80%
	OPD	x	4	5		4	4		4	5	
	RAPD										
	Cannot determine		1	5					1	5	

Prediction accuracy was calculated by the formula: (number of correct predictions) / (total number of predictions) x 100%; Correct (n) = correct predictions; Total (n) = total number of predictions. OPD = open pancreatoduodenectomy; RAPD = robot-assisted pancreatoduodenectomy; N/A = not available.

Appendix 6.10 - Confidence levels regarding vascular involvement prediction

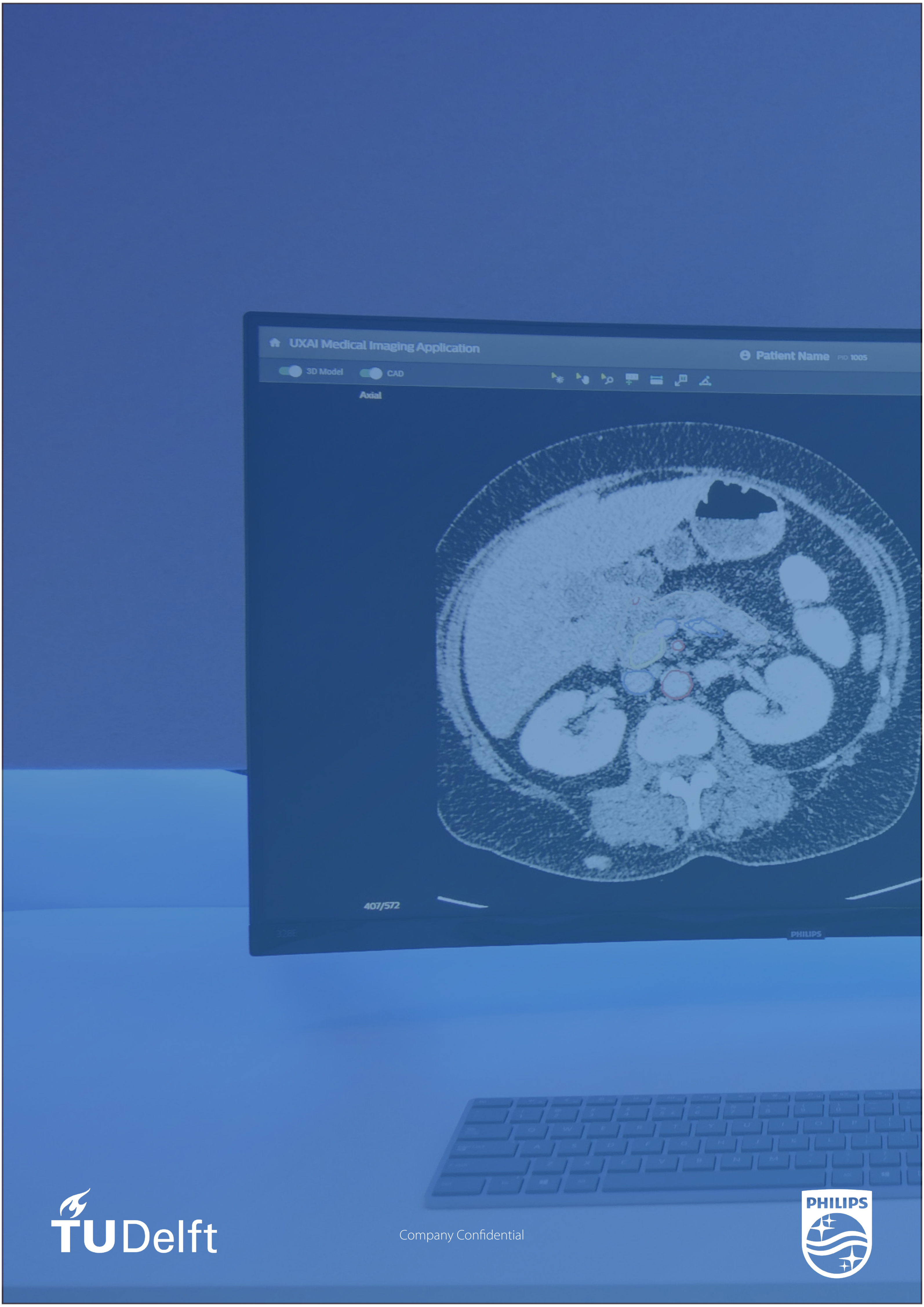
Appendix Table 6.10.1 Confidence levels regarding vascular involvement prediction

Category	CT- condition *Median [25th and 75th percentile]*	3D-condition *Median [25th and 75th percentile]*	CAD-condition *Median [25th and 75th percentile]*	CT vs 3D *p-value*	CT vs CAD *p-value*	3D vs CAD *p-value*
All cases combined						
Resectability	8 [6.25 - 9]	8 [8 - 10]	8 [7.75 – 9]	.17	.29	.94
Vascular resection	7 [6 - 8]	9 [7 - 9]	8 [6.75 - 9]	**.033***	.26	.59
Simple cases						
Resectability	9 [8 - 10]	9 [8.25 - 10]	9 [8 – 10]	.52	.96	.68
Vascular resection	8 [6.5 - 9]	9 [9 - 10]	9 [7 - 10]	.071	.43	.59
Complex cases						
Resectability	7 [5 - 8]	8 [7 - 8]	8 [7 - 8]	.21	.056	.86
Vascular resection	6 [3 - 7]	7 [6 - 8.25]	7 [6 - 8]	.23	.37	.94

Median, 25th and 75th percentiles were calculated with the Kruskal-Wallis statistical tests. P-values for comparing different conditions were calculated by performing multi-comparison testing. *p-value < .05; **p-value<.001.

Appendix Table 6.10.2. P-values regarding the confidence levels of simple compared to complex cases

Category	CT-condition p-value	3D-condition p-value	CAD-condition p-value
Resectability	**.0054***	**<.001****	**.029***
Vascular resection	**.0086***	**<.001****	**.0069***


UXAI Medical Imaging Application
Patient Name
3D Model
CAD
Axial
407/572
PHILIPS