Chapter

Computer Assistance in the Minimally Invasive Ablation Treatment of Pancreatic Cancer

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Abstract

The insertion of ablation needles towards pancreatic tumors demands excellent anatomical knowledge and interdisciplinary skills from the medical professional. While the placement of a single needle next to the structures at risk surrounding the pancreas is considered a challenging task, irreversible electroporation requires multiple needles to be placed in parallel at a specific location. Minimally invasive procedures complicate the already ambitious procedure, yet the ablation method bears potential to increase the overall survival for patients with locally advanced pancreatic cancer. Current studies require more clinical evidence regarding the efficacy of irreversible electroporation in pancreatic cancer by means of randomized controlled, multicenter trials. However, the ablation treatment is currently applied in expert centers only, which is due to the complex task of the needle placement. Computer-assisted surgery has shown its potential in different fields of applications to improve the targeting of diseased tissue and the confidence of the medical professional. The application of computer-assisted needle navigation for pancreatic cancer ablation holds the prospect to make the procedure more reproducible and safer.

Keywords: pancreatic cancer, needle guidance, irreversible electroporation, Computer-assisted surgery

1. Introduction

Pancreatic cancer is one of the most aggressive types of cancer in the abdominal cavity with poor survival rates below 10% [1]. The reasons for the poor prognosis range from late detection of the cancer, vascular invasion, and difficult access due to the surrounding structures at risk. Attributable to the late detection, 80% of patients are not eligible for resection as they are diagnosed with locally advanced (30%), or metastatic pancreatic cancer (50%) [2]. Patients with locally advanced pancreatic cancer can benefit from alternatives such as radiotherapy, high-intensity focused ultrasound (HIFU), or ablation as a complementary treatment. Over the last decade, local ablative techniques have been used more frequently in patients without metastatic disease. Several techniques, all of which were primarily introduced in order to ablate liver metastases are in clinical use. Radiofrequency or microwave ablation, the two most widely established techniques, use thermal energy. However, high temperatures not only destroy tumor tissue but also increase morbidity if applied too close to structures such as bile duct, portal vein, superior mesenteric vein, celiac artery, or superior mesenteric artery, which all run in close proximity to the pancreas [3–5]. On the other hand, irreversible electroporation (IRE) leads to cell death by using high-voltage electrical pulses without destroying vascular collagen [6]. IRE, in contrast to thermal ablative techniques, always requires at least two needles, and metallic implants and cardiac arrhythmias are contraindications for this technique [6]. Possible morbidity arises either from needle tract injuries (bleeding, local infection due to intestinal puncture) or from energy application-associated thrombosis or necrotic tissue leading again to infection.

Local ablative techniques are generally used in the context of a multimodal treatment. Preoperative chemotherapy has been established in the most recent years for the multimodal treatment of borderline resectable and locally advanced pancreatic cancer to increase resectability [7]. Neoadjuvant chemoradiation has also been increasingly performed with favorable long-term outcomes [8]. However, response to these treatments cannot be evaluated adequately using radiologic criteria so far, thus directing decision-making regarding resection [9]. Similarly, IRE for pancreatic cancer has been facing the same problems, lacking reliable radiologic and clinical markers for the detection of response. Nevertheless, current studies have indicated that the antitumoral efficacy of IRE may be identified using immunological parameters supporting the oncological benefits of IRE, additional to the electroporative effects of this ablative method on tumor cells [10, 11].

Neoadjuvant treatment for borderline resectable or locally advanced pancreatic cancer may allow resection in up to 78% of selected patients [12]. In this case, R0 resection status has been previously described as essential to reduce local and systemic recurrence and prolong survival [13]. However, due to local extension of tumor to involve vascular structures, R0 resection is more difficult to be achieved in patients with advanced disease and positive resection margins have been frequently been underestimated [14]. Therefore, in advanced disease, multimodal treatment concepts including induction therapy, followed by resection and concomitant IRE at the surgical margins have been proposed [15]. Several studies have shown the safety and feasibility of margin accentuation with intraoperative IRE during resection for borderline resectable and locally advanced pancreatic cancer. According to this concept, intraoperative IRE before complete transection could accentuate the negative-margin dissection of the retroperitoneal margin and its surrounding perivascular soft tissue as well as the perineural and mesenteric tissue adjacent to critical vascular structures [16, 17].

Additionally, current studies have even provided most promising results in terms of reduced local and distant progression, and superior overall survival when pancreatic resection and IRE are combined [16, 17]. Careful selection of patients eligible for this strategy, together with modern systemic therapy regimens, may increase resectability and improve oncological outcomes in the near future [18].

In patients with borderline resectable and locally advanced pancreatic cancer, IRE was also identified as a valuable tool to offer consolidative disease control and symptom relief such as pain control and to support eradiation of the malignant lesion [19]. However, only few studies have evaluated the quality of life following IRE for pancreatic cancer [20]. In a recent study, 84 patients undergoing IRE for locally advanced pancreatic cancer were enrolled. Quality of life assessment indicated that IRE therapy does not impair the quality of life in the short term. Adverse post-interventional events such as increased insomnia and constipation at 3 months and diarrhea at 6 months after IRE are most probably related to other clinical factors such as chemotherapy-associated toxicity. Therefore, IRE is not expected to adversely affect long-term quality of life in this patient cohort [21]. Further studies are required to examine quality of life following IRE in the long term.

The latest numbers on published pancreatic IRE cases investigated by Moris et al. [22] counted a total of 498 treatments and accentuate the lack of clinical evidence as an indicator for low numbers in pancreatic IRE treatments compared to other fields of application. While the procedures were either conducted percutaneously (n = 232) or open (n = 262), the laparoscopic approach (n = 4) played only a minor role [22].

IRE application requires the user to place the needles within a certain distance and angle to each other [23]. This makes the use of the ablation technique very difficult, especially when navigating the needles close to structures at risk. With respect to the laparoscopic needle placement, the long needles and decreased field of view add additional complexity to this task.

2. Navigate the pancreas

The workflow for pancreatic IRE treatments is divided into a preoperative planning and intraoperative navigation phase.

2.1 Preoperative needle planning

Tomographic images are acquired to identify the structures at risk in proximity to the tumor. These structures include vessels, bile ducts, and organs as visualized in **Figure 1**.

To assess suitable patients for the IRE treatment, patients are screened to determine possible access windows and the needle configuration depending on the treatment approach [24]. In addition, 3D reconstructions derived from the original images enhance the spatial understanding during the planning of the trajectories.

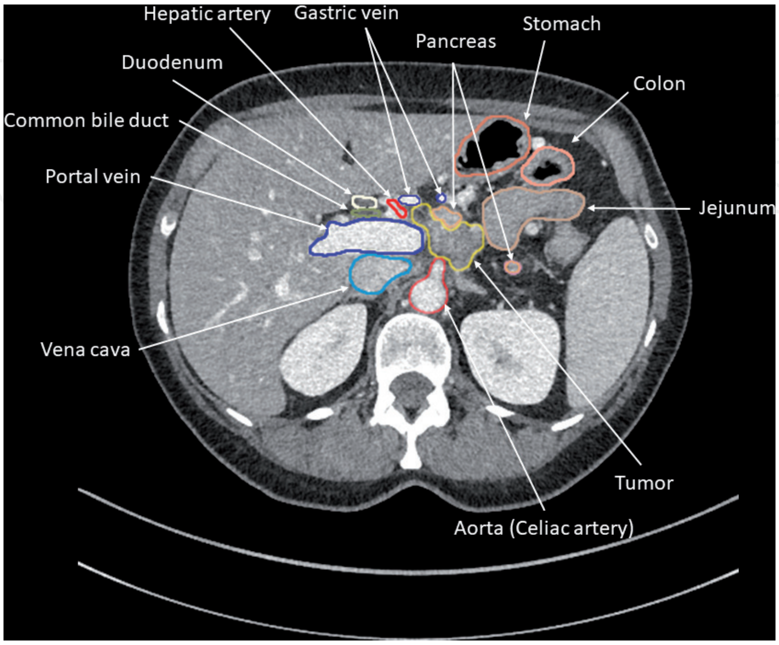

Figure 1.
Axial computed tomography image of a patient with LAPC where the tumor encapsulates the celiac artery.

However, information regarding the preoperative IRE planning phase remains sparse in current literature.

2.2 Intraoperative needle placement

While the surgical (open or laparoscopic) approach provides advantages to mobilize the structures at risk to gain a better access window for the needles, the review of all eligible studies until August 2018 identified a morbidity of 36% for the surgical approach (89/247) compared to 24.3% for the percutaneous IRE approach (56/230) [22].

Atraumatic needle placement is key for a successful treatment outcome; thus, the needles need to be monitored with computed tomography (CT), magnetic resonance imaging (MRI), fluoroscopy, or with live ultrasound (US) depending on the treatment approach. As of today, there is no comparative study investigating CT vs. US-guided IRE needle placement. Both modalities may be used to check for proper needle placement [19, 25, 26]. However, since preoperative planning is typically conducted on CT images, it may be considered as the primary modality for guiding needle placement during the percutaneous intervention. The main disadvantage of increased radiation can be considerably reduced by complementing computer-assisted navigation, as will be discussed later [27]. In addition, CT-guided procedures are less dependent on the experience of the user and offer the possibility to check immediately for post-interventional complications such as bleeding or thrombosis [27, 28].

The flexibility of the needles represents an additional challenge to keep the needles on track during the insertion. Dedicated hardware tools provide additional support to guide the needle to the specific location by reducing bending artifacts. The most basic form of needle guidance is the usage of the needle spacer provided by AngioDynamics (Latham, New York) to achieve the desired interelectrode distance, yet it does not prevent the needle from bending during the insertion [29]. Martin et al. [30, 31] emphasize the usage of a needle guide attached to the biplanar US probe for more precise needle placement and to keep the needle in the ultrasound plane. However, this approach limits the spatial freedom of the ultrasound transducer due to the static properties of the guide and aggravates the monitoring of structures at risk.

3. The doctor's opinion

To elaborate on the necessity of dedicated planning and navigation assistance, we conducted a questionnaire with eight medical doctors (MDs). The study population consisted of MDs with specialty in HPB surgery (n = 7) and surgical oncology (1) active in USA (1), India (1) Turkey (1), Germany (1), Austria (1), and Switzerland (3). The MDs performed between 30 and 120 pancreatic surgeries annually (average value of 70 surgeries per year). The yearly number of IREs was situated between 0 and 20 treatments with an average number of 4.5. All questioned doctors performed the preoperative planning of IRE cases solely on tomographic images and occasionally in combination with reconstructed 3D models. Due to the complex anatomy with varying patient-specific structures at risk, all MDs argue in favor of a preoperative IRE planning tool, which makes use of imaging data in combination with reconstructed 3D models to verify the feasibility of needle configurations. Most of the pancreas specialists see a need for minimally invasive pancreas IRE (87.5%) as well as for intraoperative needle navigation (100%) (illustrated in **Figure 2**) [32].

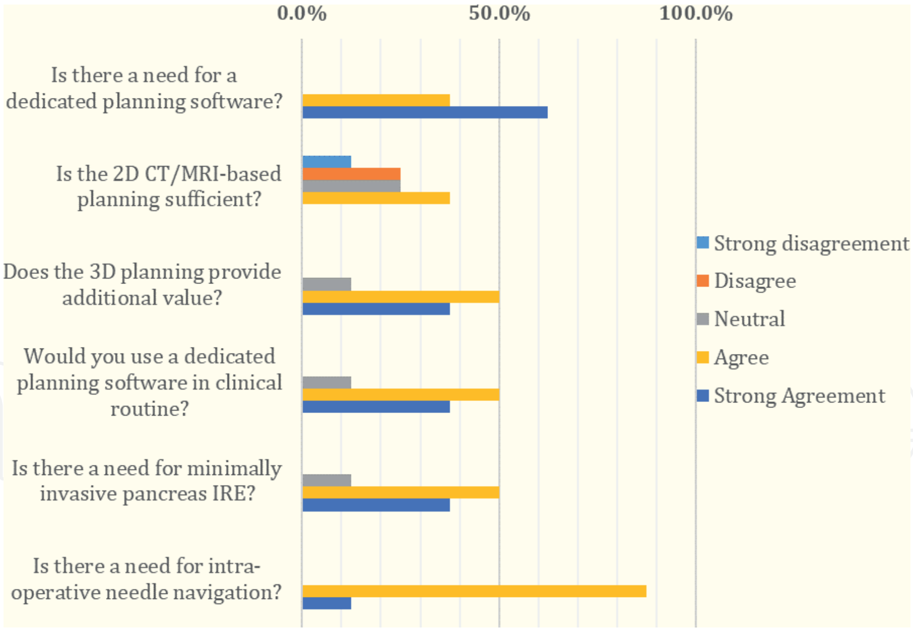

Figure 2.
Result from questionnaire where the need for dedicated tools is highlighted to assist the clinician in the perioperative procedure.

4. Computer-assisted needle guidance

Computer-assisted surgery (also known as stereotactic surgery) is established in fields like orthopedics and neurosurgery and emerged from “being just around the corner” to clinical routine of abdominal surgery over the recent decade [33]. When it comes to needle guidance, Beerman et al. [34] have reported the experiences from 1000 consecutive cases using computer-assisted image-guidance in liver ablations. The key message of this study is the necessity of navigation solutions with respect to reproducibility in percutaneous, laparoscopic, and open interventions [34]. Another report investigating the accuracy between guided and manual probe placement shows a significant advantage for the guided approach [35]. Martin et al. [36] discuss the advantages of computer assistance in the placement of single needles during a liver phantom study demonstrating that 95% of the participants were able to hit the center of the tumor using the computer-assisted approach compared to 65% with ultrasound (US) only.

The system used in the above studies was designed by CAScination (Bern, Switzerland) and provides guidance for interventional and surgical liver procedures (see **Figure 3**).

With regard to minimally invasive applications the system discriminates between the percutaneous and laparoscopic approach in the following aspects:

4.1 Percutaneous ablation

The navigation system supports the clinician during percutaneous ablation, which is performed in the intervention suite using computed tomography (CT) or cone-beam CT (CBCT) imaging. The patient is under general anesthesia with respiratory motion control and positioned on a vacuum mattress. Retroreflective single markers are attached to the patient’s skin using a dedicated marker template. The single markers are detectable by the optical tracking camera and in the tomographic images and build the foundation for virtual to physical space registration. Furthermore, their spatial position is used for monitoring of patient movement throughout the procedure. The needle trajectories are then planned, navigated, and verified using CT images, with the possibility of planning IRE needle configurations (**Figure 4**).

Figure 3.
Setup for percutaneous needle insertion. Aiming device (A), touch monitors (B), optical tracking camera (C), patient markers (D).

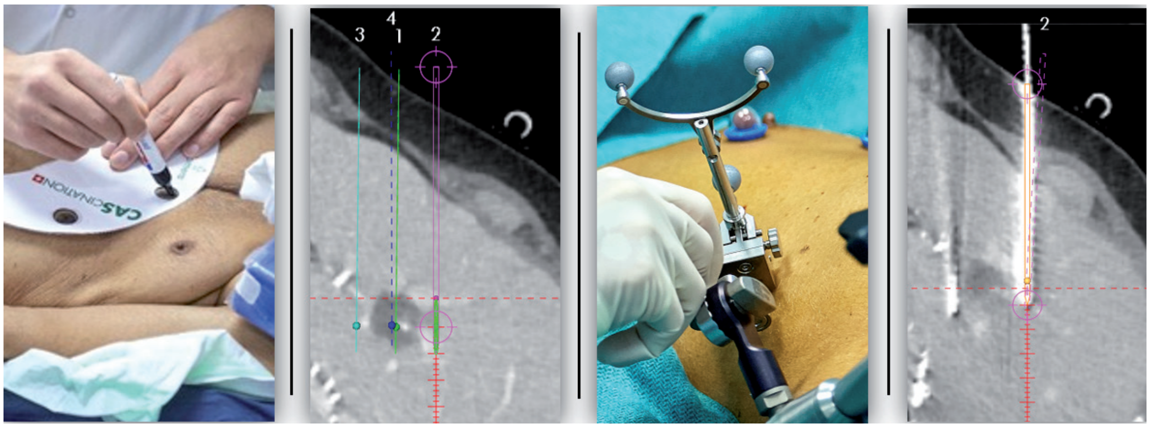

Figure 4.
Percutaneous workflow from left to right: Patient marker attachment, CT-based IRE trajectory planning, positioning of aiming device, and needle placement control.

For the initial planning image, contrast-enhanced CT is the preferred choice to achieve a good discrimination between the structures of interest. To further enhance the planning procedure, a preoperative MRI image can be fused with the intraoperative image data to visualize structures not traceable in the intraoperative CT.

Lachenmayer et al. [37] retrospectively analyzed the system in 174 percutaneous ablations of hepatocellular carcinoma (HCC) and reported a median lateral error of 3.2 (0.2–14.1) mm. They concluded that percutaneous, computer-assisted needle navigation is safe and efficient for treatment of HCC. Beyer et al. [38, 39] evaluated the system against manual, CT-fluoroscopically guided probe placement for IRE of liver tumors. The CAScination guidance ($n = 10$) was compared against manual guidance ($n = 10$) and they reported a significant decrease in planning time (55 vs. 104 min, $P < 0.001$) and radiation exposure. The procedural accuracy, measured as the deviation of the IRE electrodes with respect to a defined reference electrode, was significantly higher for the navigated approach (2.2 vs. 3.3 mm mean deviation, $P < 0.001$) [39].

4.2 Laparoscopic ablation

The system for laparoscopic needle navigation relies on a surface landmark registration in which distinct points on the organ surface are sampled with tracked instruments and matched with the corresponding points from available patient image data. These data include preoperative CT images with optional 3D reconstructions from structures of interest. Guidance is achieved by tracking of the ablation needle using retroreflective markers attached to the hand piece (**Figure 5**).

A major drawback for the surface landmark-based registration approach is organ deformation due to pneumoperitoneum, which downgrades navigation accuracy on preoperative image data. Intraoperative CT imaging would help to reduce deformation artifacts; however, this requires the availability of a hybrid OR [40]. Prevost et al. [41] investigated the laparoscopic guidance solution for liver resection and ablation in 10 cases with the main conclusion being that the navigation system enhances the explorative phase, yet the registration accuracy was not sufficient for reliable tool navigation. Stillström et al. [42] pioneered in the application of computer assistance in laparoscopic pancreas IRE. They reported the feasibility of image-guided navigation in the operating theater even though the system was mainly used for orientation purposes.

4.3 Needle guidance

The CAScination system distinguishes between two approaches for needle guidance, namely active and passive guidance. The active guidance (freehand approach) makes use of instrument calibration to determine the needle tip with respect to the marker shield attached to the hand piece of the needle, whereas passive guidance makes use of a tracked mechanical arm (aiming device approach) which is pre-calibrated due to known geometric properties. While the former provides the advantage of visualizing the needle tip during the insertion to obtain an active depth control, it is affected by errors resulting from the calibration and needle bending. The latter is not affected by the calibration error and reduces the bending artifacts by means of brackets guiding the needle along the oriented path. During needle insertion, the lateral deviation from the original plan is of high significance as it may require needle repositioning. Wallach et al. [43] compared the two approaches during a phantom study with 25 needle punctures on a nonrigid phantom. The resulting lateral error of the needle to the defined target was found to be significantly lower with the aiming device (2.3 ± 1.3 mm vs. 4.2 ± 2.0 mm) [43].

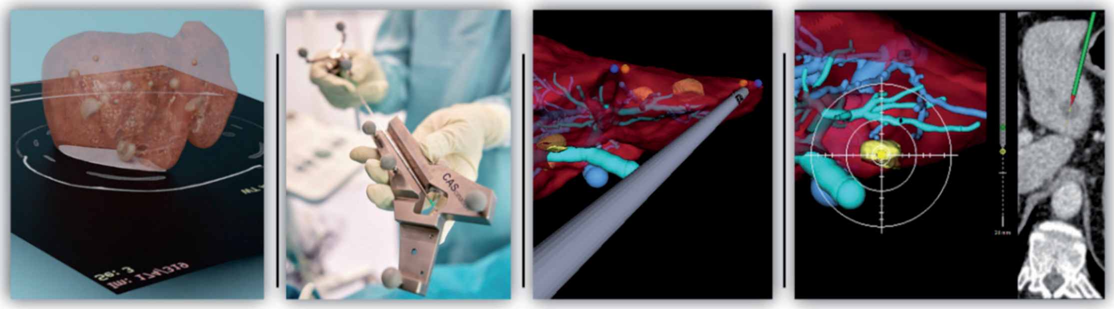

Figure 5.
Laparoscopic workflow from left to right: preoperative image segmentation, optical instrument calibration, landmark-based registration, targeting with active depth control.

4.4 Alternative navigation solutions

There are a number of navigation solutions for abdominal organs on the market. These devices share the same fundamental functional principles and provide a different range of functionalities, which can be used in the setting of IRE on the pancreas. Given the high accuracy requirements and the complexity in needles placement relative to a number of risk structures, we deem functionality for multi-needle planning as well as accurate needle guidance as mandatory requirements for navigated IRE on the pancreas. The following paragraphs present different available navigation solutions and evaluate them with respect to these two requirements.

The IMACTIS® CT (Imactis SAS, La Tronche, France) solution is designed for percutaneous interventions using CT imaging and electromagnetic instrument tracking. The device was applied on different target organs and available literature includes an assessment of needle positioning accuracy and time requirements in a prospective randomized trial. The median Euclidean error [interquartile range] using the computer-assisted approach was found to be 4.1 mm [2.7–9.1 mm] compared to 8.9 mm [4.9–15.1 mm] for the non-navigated group for a total of 120 patients [44]. This shows that IMACTIS® CT has the potential to reach sufficient accuracy for IRE needle placement. Its shortcoming with respect to the application of pancreatic IRE lies in the fact that the device has no functionality for needle planning and multi-needle treatments.

The MAXIO (Perfint Healthcare, Florence, Oregon, USA) is used in CT-guided, percutaneous interventions and includes a robotic arm for needle placement. The device comprises a planning software supporting single- as well as multi-needle planning for different needle types. Beyer et al. [38] investigated the MAXIO with respect to procedural accuracy in a retrospective study of 40 cases of liver IRE conducted by an experienced interventional radiologist. Out of these, 19 were conducted using manual needle placement under CT fluoroscopy guidance and 21 with guidance of the robotic system. To calculate the procedural accuracy, an oblique slice was placed at the needle tip closest to the tumor with the normal pointing along the needle direction. Each needle tip was successively projected on the slice translated 3 cm from the tip toward the hand piece to calculate the distance to the needle center. The resulting accuracy was significantly improved when comparing the robotic approach to freehand needle placements (2.2 vs. 3.1 mm) [38].

The navigation system Explorer (Pathfinder) is designed for needle guidance in open liver surgery and is based on optical instrument tracking (same functional principle as CAS-One for the laparoscopic use case). A study by Bond et al. [45] investigated needle guidance accuracy and required time in a randomized controlled trial of IRE for pancreatic cancer. The application of the Explorer device decreased time for needle placement from 20 to 11 min while reaching an accuracy of 3.4 mm in relative spacing between the needles. The accuracy of needle placement with respect to the target anatomy is expected to be lower as the publication reports average fiducial registration errors of 10.8 mm. The authors conclude that the main benefit of the navigated approach is the increase of the surgeon's confidence to localize the needle using stereotactic navigation. The image to physical space registration is seen as the biggest obstacle to achieve a reliable overlay between the preoperative plan and the intraoperative scene.

Further guidance solutions for pancreatic IRE potentially include the use of ultrasound fusion devices such as those used in percutaneous ablation treatment on the liver. While providing needle guidance under real-time feedback, there are no devices providing multi-needle planning functionality together with ultrasound-based needle navigation. To our knowledge, there are no reports on the usage of ultrasound-fusion and navigation devices in the setting of pancreatic IRE.

5. Computer-assisted pancreas navigation

Existing computer-assisted navigation solutions address the needs of the pancreatic MDs to some extent, yet there remains room for improvement. The application of IRE as a treatment for pancreatic cancer bears additional challenges, which are partially covered by existing solutions:

- The IRE needle configuration is dependent on the tumor size. The optimal spacing between two IRE probes shall be situated between 1.5 and 2.5 cm to achieve a successful treatment outcome [23].
- Multiple structures at risk surrounding the pancreas require the probes to be planned and placed according to safety criteria to reduce insertion related complications [22, 25].
- The flexible IRE needles increase the risk of deformation during the insertion process.
- A homogeneous ablation field along the active zone of the IRE needles is dependent on the parallelism of the inserted needles [46].

Low usage numbers of stereotactic needle guidance in the pancreatic use case highlights that not all problems have yet been addressed to support the complete perioperative procedure. A study recently published by He et al. [47] demonstrated the feasibility of robot-assisted percutaneous IRE treatment of pancreatic head cancer in 9 cases. With respect to spatial accuracy, the stereotactic percutaneous navigation outperformed the stereotactic laparoscopic navigation in existing reporting. Therefore, stereotactic percutaneous needle guidance can be seen as the foundation to achieve reliable and reproducible navigation results. Yet, it only constructs one part of a dedicated computer-assisted pancreatic IRE workflow.

5.1 IRE planning tool

Preoperative image data are essential to generate a safe and feasible ablation plan with an optimal needle configuration to treat the tumor. We developed a dedicated preoperative planning tool, which makes use of CT/MRI image data in combination with 3D reconstructions to simulate IRE needle configurations. The tool allows the MD to define target and entry positions on multiplanar reconstructions (MPR) of the tomographic images with the possibility to select different needle configurations (layout and spacing). Under consideration of IRE-related constraints (spacing and parallelism), the trajectories can be optimized to cover the region of interest. The segmentations are conducted by a radiologist using dedicated software and can be tailored upon the type of intervention. Unlike for the open approach, preoperative segmentations for a percutaneous approach could include structures like the stomach, colon, or liver as well. This information is beneficial for the determination of the access window and to evaluate risk structures in the vicinity of the needles.

The planning tool was evaluated in the course of a clinical study of IRE in a laparotomy setting at the local hospital (Inselspital, Bern, Switzerland). **Figure 6** demonstrates the application of the planning tool to 1 out of 10 cases. During the surgery, the decision was to place the needles according to plan # 1 as the superior mesenteric vein was not mobilizable enough to obtain a window for the inferior right needle in #2. The 3D planning tool proved beneficial in both the preoperative

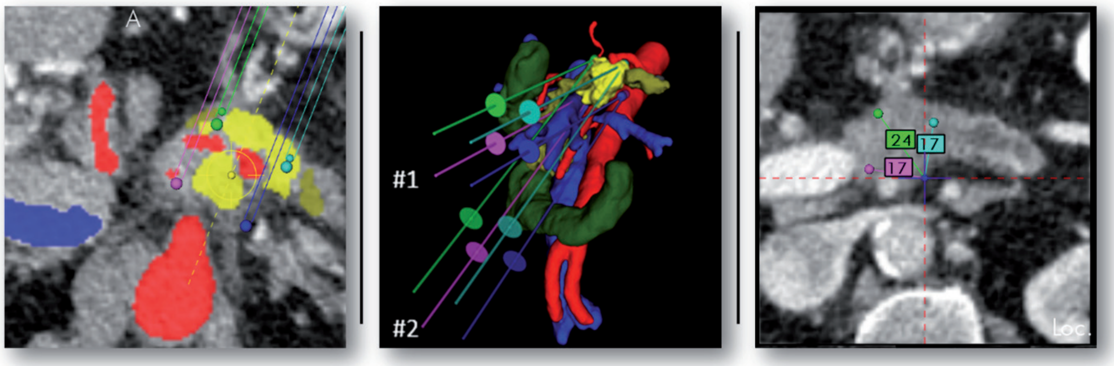

Figure 6.
Preoperative plan on axial plane with segmentation overlay (left). Two IRE configurations with 3D reconstructions (middle). Image plane at needle tip in direction of the trajectory to visualize distances between the needles in millimeter (right).

as well as intraoperative phase as it increased the MDs spatial understanding during the generation of the ablation plan.

5.2 Aiming for parallelism

To transfer the predefined ablation plan from theory to practice, a navigation system can take remedial action. Visual guidance information provided by the navigation system aids the clinician to position the ablation needle relative to the defined path. The computer-assisted navigation solutions proved to be advantageous for IRE needle guidance in terms of procedural accuracy compared to the manual, CT-fluoroscopically guided approach [38, 39]. Whereas these navigation systems make use of a mechanical guide, navigation systems such as the IMACTIS$^{®}$ CT require the user to actively align and insert the needle. This might cause a challenge for less experienced clinicians in needle guidance. We have therefore compared the two computer-assisted navigation approaches discussed in Section 4.3 by means of a phantom study with a similar setup as in [43]. Firstly, the needle was actively tracked (freehand approach), and secondly the mechanical arm (aiming device approach) was used. Seven participants were requested to place three needles (17 g, 15 cm) using each approach around a tumor encompassing the celiac artery in an artificial, flexible phantom. Three trajectories were predefined on the navigation system and each user received an instructional training. The calibration procedure for the freehand approach was conducted upfront to minimize the calibration error. The starting sequence was randomized, the needle control scan was conducted with a mobile C-arm, and the validation again conducted with the CAScination system by means of image to image fusion.

The mean lateral error for the aiming-device approach (2.4 ± 0.7 mm) was found to be similar compared to the lateral error (2.3 ± 1.3 mm) obtained in [43]. The error for the freehand approach resulted in a larger mean error (6.7 ± 1.7 mm) compared to the results from [43] (4.2 ± 2.0 mm), which can be explained by the larger group of participants with varying experience in manual needle placement. Parallelism of the needles for both approaches was calculated according to the method used in [38] where an oblique slice was placed at the needle closest to the tumor with the normal pointing along the needle direction. Each needle tip was successively projected on the plane translated 3 cm from the tip toward the handpiece to calculate the distance to the needle center. With a total of 14 samples per approach, the resulting mean Euclidean error was significantly lower for the aiming device than for the freehand approach (1.5 ± 0.7 mm versus 2.4 ± 1.1 mm) with a p-value of 0.014 (see **Figure 7**). However,

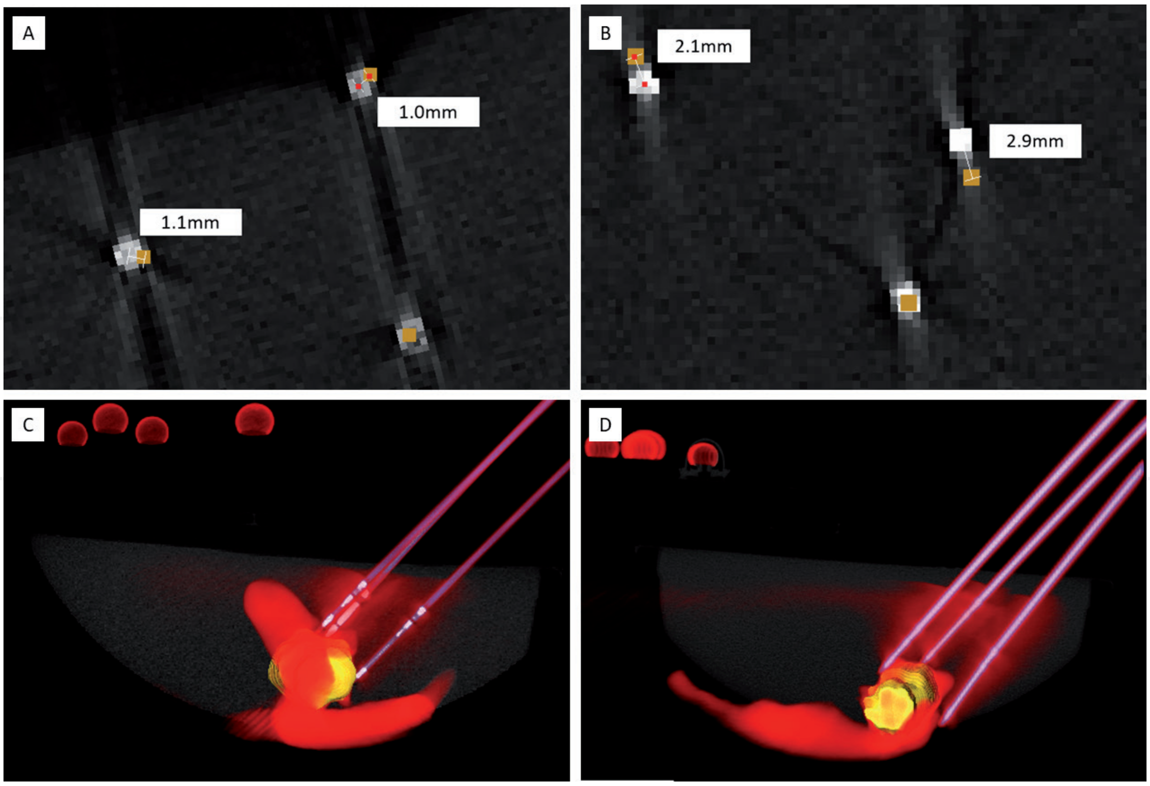

Figure 7.
Comparison of aiming device versus freehand for a specific participant. The top row visualizes the calculation of the Euclidean error between the aiming device (A) and freehand (B) approach. Volume rendering from control CT of aiming device (C) and freehand (D) guidance highlights the bending of the needle in the freehand approach.

these results should not be compared with the findings by Beyer et al. [38, 39] due to the setup of the studies (phantom vs. in vivo), yet their reported decrease of the error using the computer-assisted navigation goes along with the findings by our group.

6. Future directions of IRE in pancreatic cancer

Given the severity and decreased overall survival of patients diagnosed with locally advanced pancreatic cancer, there is a driving need for treatment alternatives to conventional chemo/radiation therapy. The minimally invasive application of IRE shows potential regarding an increase of the progression-free survival time and quality of life [48]. However, these interventions require highly experienced medical professionals as needles need to be navigated close to multiple structures at risk. Computer assistance plays a major role in all types of procedures where spatial accuracy needs to be delivered in order to achieve a successful treatment outcome. As mentioned in Morris et al. [22] there is a need for multicenter, randomized, prospective trials to determine the efficacy of IRE treatment in the pancreatic use case. To conduct IRE treatments on the pancreas, computer assistance holds the potential to standardize the workflow and to enable highly accurate needle placement independent on outstanding multidisciplinary skills, which are typically found in high expert centers.

6.1 Patient screening

The evaluation of suitable patients for IRE is a crucial step to achieve a positive treatment outcome. The Miami Protocol lists patients' criteria including among others the performance status, lesion size, and access path [24]. An important criterion is stated by the access path, which requires an excellent radiological understanding due to the difficulty of planning multiple trajectories solely on tomographic images. This coincides with the opinions of the MDs who consider conventional 2D planning to be insufficient. A dedicated planning tool would enhance the preoperative procedure as multiple access paths can be planned relative to the patient's anatomy and structures at risk better identified. This requires precise anatomical segmentations from the radiological department, which is, especially for the pancreatic use case, a time-consuming task.

6.2 Artificial intelligence-driven segmentation

To plan multiple trajectories, especially in a percutaneous fashion, multiple organs surrounding the pancreas need to be considered. To obtain a good spatial understanding of the acquired tomographic images, 3D representations from the structures of interest help in the decision-making process. Where time may be sufficiently available in the preoperative phase, it is a valuable asset during the intraoperative phase. Therefore, a compromise between accuracy and processing time must be chosen to enable 3D reconstruction from intraoperative tomographic images. Deep learning-based segmentation has shown its potential in multiple fields including medical imaging tasks [49]. Segmentation of the pancreas is seen as a challenging task due to the dependency on good delineation of the organ to its adjacent structures in the abdominal cavity [50]. To segment the complete range of structure needed for pancreas IRE planning, Roth et al. [51] describe a multi-scale pyramid of 3D fully convolutional network. The reported network was trained and validated using 377 clinical CT datasets with annotated organs and vessels. The performance of the system was measured by means of the DICE score, which represents the similarity between the automatic segmentations from CT images not used for training and their manual annotations. The network was able to achieve a Dice score close to 90% on average, which holds promising aspects for automatic, intraoperative segmentation [51].

6.3 Automatic trajectory optimization

Based on the patient-specific data, automatic trajectories can be computed according to permitted access paths while securing a specific distance to structures at risk [52]. The optimization for the IRE use case would further depend on the needle configuration, interelectrode spacing, and parallelism constraints.

6.4 Ablation zone prediction

The application of IRE lacks the possibility of ablation validation as, in contrast to thermal ablation, the ablation zone cannot be monitored in real time. Therefore, the clinician must fully rely on the ablation zone prediction from the manufacturer, which is based on mathematical and ex vivo models. However, ultrasound elastography has shown potential to distinct ablated tissue from normal liver parenchyma with respect to tissue stiffness, which peaked 4 hours post-ablation [53]. Based on the ultrasound characteristics at 2 hours post-ablation in combination with histopathology findings, Bhutiani et al. [54] have shown the mismatch of current models with in vivo-generated ablation volumes in porcine liver and spleen.

6.5 From theory to practice

The placement of needles according to the defined trajectories is seen as a challenging task, especially for medical professionals who are not versatile in the art of needle insertion. Therefore, navigation solutions are of great interest to empower these clinicians to conduct safe procedures with IRE in the pancreas. Needle navigation by means of software and hardware guidance is best applicable to improve the spatial accuracy and to spare structures at risk. Especially the aiming device has shown its value in the reduction of needle bending for inexperienced users. Further improvement toward parallel insertion of the electrodes is required since this is, next to the interelectrode spacing, an important aspect to achieve a homogeneous ablation volume.

7. Conclusion

Minimally invasive ablation treatment of locally advanced pancreatic cancer is a promising, yet challenging task. The application of the IRE as a treatment addition to conventional chemotherapy with optional radiotherapy has the potential to increase the overall survival, which needs further investigation upon its efficacy by means of randomized-controlled, multicenter studies. The percutaneous application of IRE demands a sophisticated workflow from preoperative screening of suitable patients to intraoperative implementation of the predefined ablation plan. Computer-assisted surgery systems can aid the clinician during these steps with dedicated software and hardware tools to achieve reproducible and effective treatments.

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Conflict of interest

Benjamin Eigl is employed as a PhD student at CAScination, with his salary covered by the European Union’s Horizon 2020 Research and Innovation programme. Matthias Peterhans is the CSO and cofounder of CAScination. Stefan Weber is CEO and cofounder of CAScination.

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