A phantom to simulate organ motion and its effect on dose distribution in carbon ion therapy for pancreatic cancer

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\section*{Abstract}

\textbf{Objective.} Carbon ion radiotherapy is a promising radiation technique for malignancies like pancreatic cancer. However, organs’ motion imposes challenges for achieving homogeneous dose delivery. In this study, an anthropomorphic Pancreas Phantom for Ion-beam Therapy (PPIeT) was developed to simulate breathing and gastrointestinal motion during radiotherapy. \textbf{Approach.} The developed phantom contains a pancreas, two kidneys, a duodenum, a spine, and a spinal cord. The shell of the organs was 3D printed and filled with agarose-based mixtures. Hounsfield Units (HU) of PPIeTs’ organs were measured by CT. The pancreas motion amplitude in cranial-caudal (CC) direction was evaluated from patients’ 4D CT data. Motions within the obtained range were simulated and analyzed in PPIeT using MRI. Additionally, GI motion was mimicked by changing the volume of the duodenum and quantified by MRI. A patient-like treatment plan was calculated for carbon ions, and the phantom was irradiated in a static and moving condition. \textbf{Main results.} PPIeT presented tissue equivalent HU and reproducible breathing-induced CC displacements of the pancreas between (3.98 ± 0.36) mm and a maximum of (18.19 ± 0.44) mm. The observed maximum change in distance of (14.28 ± 0.12) mm between pancreas and duodenum was consistent with findings in patients. Carbon ion irradiation revealed homogenous coverage of the virtual tumor at the pancreas in static condition with a 1\% deviation from the treatment plan. Instead, the dose delivery during motion with the maximum amplitude yielded an underdosage of 21\% at the target and an increased uncertainty by two orders of magnitude. \textbf{Significance.} A dedicated phantom was designed and developed for breathing motion assessment of dose deposition during carbon ion radiotherapy. PPIeT is a unique tool for dose verification in the pancreas and its organs at risk during end-to-end tests.
1. Introduction

Pancreatic cancer is one of the deadliest cancers worldwide and it progresses aggressively with a five-year survival rate of 2%–9% (McGuigan et al 2018, Rawla et al 2019, Mitchl et al 2021). Its treatment options are scarce, and the best potential curative treatment is complete resection (Doi et al 2008). However, 80% of pancreatic cancer patients are diagnosed in a locally advanced or metastatic state, suffering from unresectable cancer. In non-metastasized unresectable cases or as a neoadjuvant therapy concept, radiotherapy can improve local tumor control (Chang et al 2009, Mahadevan et al 2010, Yovino et al 2011, Hammel et al 2016, Versteijne et al 2022). Nevertheless, factors such as motion induced by breathing can lead to an inaccurate dose delivery during radiotherapy, increasing the potential exposure of the organs at risk (OARs). In pancreatic cancer treatment, the main OARs are the kidneys, the duodenum and the spinal cord (Hassanzadeh et al 2021, Liermann et al 2021).

Among different radiation techniques, pancreatic cancer patients presented promising results when treated with carbon ions (Kawashiro et al 2018). A favorable outcome with a 47% overall survival rate after 2 years was shown, compared to 36% when using intensity-modulated radiation therapy with high-energy x-rays (Krishnan et al 2016). Following these results, multiple prospective clinical trials testing carbon ion radiotherapy in pancreatic cancer are currently being conducted (Vitolo et al 2019, Liermann et al 2022). Nevertheless, inconsistencies between planned and delivered doses in carbon ion radiotherapy can be large due to variations of depth-dose distribution, even when considering small spatial displacements of the target (Fontana et al 2016). Additionally, organ motion can lead to underdosage of the target volume and over-dosage of the OARs (Phillips et al 1992, Bert et al 2008).

The pancreatic motion is highly variable, where values from 1.0 mm up to 27.3 mm in the craniocaudal (CC) direction were found (Bhasin et al 2006, Knybel et al 2014, Dolde et al 2019a, Jing et al 2021). Although motion management strategies have improved pancreatic treatment outcomes, these often impose unease on the patient by the obligation of breath holding or wearing a corset (Dolde et al 2019a). Additionally, gastrointestinal (GI) motion is a challenge during carbon ion radiotherapy since it causes internal anatomic variation during dose delivery. In fact, peristalsis and gas accumulation make it difficult to deliver a homogenous dose to the tumor while sparing the bowel (Kumagai et al 2009). Previous studies reported relative motion differences between the pancreas and the duodenum from 13.0 up to 18.5 mm (Mostafaei et al 2018).

The use of phantoms in radiotherapy enables dose measurements by providing quality assurance (QA) procedures and allowing for the testing of new treatment scenarios without harming patients. Most of these phantoms have geometrical shapes that do not resemble the human body while anthropomorphic phantoms enable end-to-end tests in a more human-like environment (Tajik et al 2022, Vedelago et al 2022). In the last years, the development of anthropomorphic phantoms increased continuously, and specialized phantoms have gained significant attention due to their ability to simulate human-like characteristics, particularly in terms of breathing motion. This capability becomes especially relevant when considering scenarios involving the movement of tumors and OARs (Cheung and Sawant 2015, Kim et al 2016, Mann et al 2017, Ehrbar and et al 2019). Recently, the development of a phantom for liver treatment made it possible to combine breathing motion of different organs with human equivalent CT and MRI contrast to perform end-to-end studies in MR-Linacs (Weidner et al 2022). Notably, there is a growing emphasis on compatibility with MRI systems, leading to the design of phantoms tailored for optimal performance within these environments. Other authors presented a Magnetic Resonance Image-Guided Radiotherapy dynamic lung motion thorax anthropomorphic QA phantom (Steinmann et al 2019) as well as an anthropomorphic phantom developed for deformable lung and liver studies, which (Colvill et al 2020) have tackled the increasing need for MRI-compatible phantoms (Colvill et al 2020). One other phantom to be named is the Advanced Radiation DOSimetry phantom (ARDOS) which incorporates a moving rigid ribcage and can be used to measure dose during ion beam therapy (Kostiukhina et al 2017, Kostiukhina et al 2020, Lebbink et al 2022). Additionally, an anthropomorphic thorax breathing phantom was developed specifically for pencil beam scanning proton therapy (Perrin et al 2017).

The present study aims to develop a Pancreas Phantom for Ion-beam Therapy (PPIeT), in which the pancreas is the target organ, while the duodenum, kidneys, spine, and spinal cord serve as OARs. Breathing-induced organ motion within PPIeT was analyzed for different motion inputs with increasing amplitudes. In addition, the influence of the tested motion on dose distribution within the organs in carbon ion therapy was explored. Thanks to the designed features, PPIeT could be used to conduct thorough end-to-end tests for upcoming pancreatic cancer treatment with carbon ions.
2. Materials and methods

2.1. Phantom design
Based on the development of a phantom for liver treatment (Weidner et al. 2022), PPIeT was constructed out of two 51 cylindrical polypropylene containers, with a height of 26.0 cm, a wall thickness of 2 mm and a transversal ellipse shape with 29.0 cm major axis and 21.0 cm minor axis. These two containers were interlocked and had a frontal cut-out of (24.0 × 10.5) cm² for a flexible abdominal wall. This area was covered with a 3 mm thick TFC silicone caoutchouc type 6 layer with a shore of 22 (Troll Factory Rainer Habekost e.K., Germany), and clamped between the two containers. The bottom of the inner container was removed, yielding a cavity with a total volume of 6.5 l, which was filled with a 0.25% w/w superabsorber-water mixture (Schauch, Germany). The top part was covered with a diaphragm made from TFC silicon and attached to the lid with 23 screws (figure 1). The circumference of the phantom is 75 cm, in agreement with an average woman’s body.

2.2. Design and construction of the organs
The organ models were designed with anthropomorphic shapes using Inventor 2018 (Autodesk, USA) and Meshmixer (Autodesk, USA). A total of five organs were included in PPIeT, namely the pancreas, two kidneys, flexible duodenum and spine with a spinal cord. The pancreas and kidneys consist of a hollowed structure with an outer shell of 3 mm thickness 3D printed using Veroclear (Stratasys, Israel, 3D printer Stratasys J55). In each of the outer shells a cavity was designed to fit the 3D printed detector inserts. The dimensions and volume of the organs (table 1) correspond to those of humans (Brant 2006, Cheong et al. 2007). Figures 1(A)–(D) illustrate PPIeT and its organs.

The pancreas and kidney shells (figures 1(E), (F)) were filled with a mixture made from agarose, nickel-diethylene triamine pentaacetic acid (NiDTPA) and potassium chloride (KCl) to mimic human tissue within different imaging techniques and in terms of the stopping power ratio (SPR) (Elter et al. 2021). Briefly, agarose, NiDTPA, KCl, and water were mixed according to the compositions of supplementary table 1 and heated up to 80 °C. Agarose was degassed using a desiccator to 150 mbar and the mixture was used to fill the 3D printed organs via openings. Afterward, the holes were closed with a polyethylene plug with a diameter of 12.8 mm (BN 1095, TL-4-128, Bossard, Germany), and cooled down to room temperature. The outer shells were designed such that they could remain sealed containing the agarose mixture inside during the experiments.

For the spine, Diran 410MF07 (Stratasys, Israel, 3D printer Stratasys F370) was used, and one cavity was designed in each of the three vertebras to fit the 3D printed detector inserts (figure 1(G)). The spinal cord imitation made of Veroclear was fixed to the posterior part of the spine. Elastic (Stratasys, Israel, 3D printer Stratasys J55) with shore 60 served as the flexible material for the duodenum, so its volume can be modified to mimic GI motion. To mimic the human body, the duodenum was designed with a C-shape and positioned around the pancreas’ head. The hollow internal cavity of the duodenum is connected to the exterior through a polyurethane tube (Festo, Germany) of 6 mm outer diameter and 1 mm wall thickness, so fluids can be taken in or out at any time (figure 1(F)).

2.3. 3D printing of detector inserts
Pluggable detector inserts were 3D designed to fit each organ. In these detector inserts, EBT3 GafChromatic films (Ashland, USA) or a 0.03 cm³ PinPoint 31015 ionization chamber (PTW, Germany) can be inserted. Inside the pancreas insert, either the films or the ionization chamber could be fitted, while for the kidneys only a film insert was placed on the medial side. In the spine, film inserts were positioned in each of the three segments, complemented by one insert in the spinal cord. The size of each insert is reported in table 2, and an illustration of each organ with its detector inserts is shown in supplementary figure S1.

2.4. Reproducibility of organ positioning inside the phantom
The pancreas, duodenum and kidneys are attached to the diaphragm, whereas the spine is screwed to the bottom of the phantom. When the phantom is opened to exchange detector inserts, the diaphragm lid and the organs attached to it are removed. Thus, for the pancreas and kidneys, guiding pins in the CC direction were fixed to the bottom of the phantom, enabling reproducible re-positioning. Since some of the superabsorber-water mixture can be lost during this process, PPIeT was refilled with the superabsorber-water mixture to weigh 8.50 kg each time after the inserts were changed. Therefore, the phantom was not damaged while changing the inserts or applying motion. The exchange procedure can be done by a trained user in 8 min. The quantification of the organs’ re-positioning was done by repetitively opening and closing PPIeT’s lid and measuring the deviations from the original position in a 3 T MRI scanner (Biograph mMR, Siemens Healthineers, Germany) using a 3D MRI T1 vibe Dixon sequence with a resolution of (1 × 1 × 1) cm³.
Figure 1. Schematic drawing of PPIeT and its organs (A), where each organ is arranged according to the human body (B). Photo of PPIeT with a flexible abdominal wall (C). Photos of organs of PPIeT attached to the diaphragm, including the pancreas, duodenum and two kidneys (D). 3D model of the pancreas (E), the right kidney (F) and the spine (G), where the arrows indicate the position of the 3D printed detector inserts. The opening for the detector insert of the pancreas is considered the virtual tumor. Additionally, a spinal cord insert is located at the posterior side of the spine (G, white color). 3D model of the flexible duodenum, where the arrow marks the hole for a tube to fill and empty it with fluids (H).
2.5. Motor-controlled movement: fixed displacement and breathing motion

Breathing motion was simulated with a hydraulic system, including two MRI-compatible double-acting cylinders (PSK Ingenieurgesellschaft mbH, Germany). One of the cylinders was connected to a linear stage, and the other to an actuator positioned cranial from the diaphragm. The stage was moved by a Nema 23 stepper motor (EC Motion GmbH, Germany) and controlled by a PLC CX5020 (Beckhoff, Germany) using TwinCat Version 3 (TcXaeShell Version 15.0.28010.2050 D15.8, Beckhoff, Germany), as illustrated in supplementary figure S2. Therewith, fixed input displacements including 10 mm, 20 mm and 30 mm were applied. Additionally, sinusoidal breathing motions over time were used as described by Weidner et al (2022):

\[
\text{Position}(t) = A \cdot \sin^2\left(\frac{\pi t}{T}\right),
\]

where \( A \) is the amplitude, set to 10 mm, 20 mm or 30 mm, and \( T \) is the motion period set to 7 s. A video showing the breathing motion in the phantom is given in the supplements (supplementary video S1).

2.6. CT measurements for contrast evaluation

CT measurements were performed with a Definition Flash CT scanner (Siemens Healthineers, Germany). An abdominal scan with 480 mA and 120 kV was used, with a voxel size of \((1 \times 1 \times 1) \text{ mm}^3\). Average Hounsfield units (HU) were retrieved from several slices of each organ using RadiAnt Dicom viewer (Medixant, Version 2022.1.1). The CT numbers of PPIeT’s organs were compared to previously published data from humans for the pancreas, kidneys and spine, whereas the CT number of the superabsorber-water mixture was compared to the one of water (Cropp et al 2013, Lamba et al 2014, Lim et al 2014, Irie et al 2021).

2.7. MRI measurement for motion analysis

Thanks to its MRI compatibility, the position of the organs in PPIeT during motion was evaluated using a 3 T MRI scanner (Biograph mMR, Siemens Healthineers, Germany) by applying two different sequences. First, a T1 vibe Dixon sequence was applied with a 3D resolution of \((1 \times 1 \times 1) \text{ mm}^3\), a repetition time of 4.22 ms and an echo time of 1.35 ms for organ motion induced by fixed input displacements. Three independent measurements of each amplitude were then compared to 0 mm input displacement, which is the static condition of PPIeT. For this, a free medical image processing platform MITK v2021.10 was used with an affine registration algorithm (Nolden et al 2013), with the center of mass of each organ used as the position.

To measure the position of the pancreas and kidneys during breathing, a fast real-time single-slice cine sequence was used for each breathing motion input amplitude. For these acquisitions, the repetition time was 265.35 ms and the echo time was 1.26 ms. 2D images were acquired every 0.315 s with a resolution of \((256 \times 256) \text{ pixels}^2\) for a \((187 \times 187) \text{ mm}^2\) area. Organs were segmented in MITK and the center of mass of each organ over all slices was calculated to retrieve the position over time.

| Table 1. Dimensions of organs in PPIeT for height in CC direction, length in right–left (RL) direction, and thickness in anterior–posterior (AP) direction. The given values are the maximum values in each direction since the measures vary due to the anthropomorphic shape. |
|---|---|---|---|
| Organ | Height CC [mm] | Length RL [mm] | Thickness AP [mm] |
| Pancreas | 65 | 140 | 35 |
| Kidney | 106 | 64 | 40 |
| Duodenum | 145 | 138 | 36 |
| Spine | 164 | 46 | 44 |
| Spinal cord | 102 | 10 | 10 |

| Table 2. Size of inserts for each organ along with the film size and number of films fitting in each of them. |
|---|---|---|
| | Insert size [mm³] | Film size [mm²] | Number of films |
| Pancreas | 25.6 × 37.6 × 23.3 | 34.0 × 23.0 | 4 |
| Kidney | 20.0 × 50.0 × 8.6 | 37.0 × 18.0 | 4 |
| Spine | 14.8 × 42.9 × 11.5 | 29.0 × 11.0 | 4 |
| Spinal cord | 10.0 × 100.6 × 7.0 | 54.0 × 6.0 | 1 |
The filling and emptying of the duodenum were done with water and therefore its movement was realized by connecting the tube to a 50 ml syringe. For emptying the duodenum, 25 ml of the water was suctioned out of it, representing a reduction of 8.6% of its total volume, in agreement with other studies (Mudie et al 2014, Waal et al 2020). In both states, full (control) and empty, measurements with a 3 T MRI scanner (Biograph mMR, Siemens Healthineers, Germany) were conducted using a T1 vibe Dixon sequence with a resolution of $(1 \times 1 \times 1)$ mm$^3$ to measure the duodenum shape as its distance to the pancreas. To assess reproducibility, the filling and emptying procedure was repeated three times and parameters were compared with a two-tailed t-test.

2.8. Human pancreas motion analysis from patient data
For analysis of the pancreas motion in CC direction, 4D CT data from 23 patients from Heidelberg University Hospital (Heidelberg, Germany) were retrospectively analyzed. The pancreas was segmented by a radiology expert with MITK and registered using the same methodology used for the phantom. This study was performed in accordance with the ethical standards of the institutional and national research committee, along with the 1964 Helsinki Declaration and its later amendments. This study was approved by the ethics committee of the Medical Faculty of Heidelberg University (Heidelberg, Germany) under No. S-688/2020.

2.9. Carbon ion irradiation
PPIeT was irradiated with carbon ions at the Heidelberg Ion-Beam Therapy Center (HIT; Heidelberg, Germany). A treatment plan was calculated using RayStation (Version 11B (12.0.0.932), RaySearch Laboratories, USA) with the dose calculation engine Pencil beam (Version 4.4) for the virtual tumor in the pancreas head as target. In the treatment plan, the dose grid was set to 2 mm isotropically, the spot spacing was 3.6 mm hexagonal and the energy layer spacing was 3.1 mm. As usually done for patients, two beams at angles $250^\circ$ and $290^\circ$ were used. A relative biologic effectiveness (RBE)-weighted dose of 4 Gy (RBE) was planned at the target, calculated with the Local effect model 1. Constraints of a maximum of 3 Gy (RBE) were set for the duodenum, spinal cord and kidneys as done in clinics (Liermann et al 2022). During irradiation, static conditions and 30 mm input amplitude breathing motion were compared, either with the pinpoint chamber in the pancreas or EBT3 films in all organs. In the course of irradiation, the duodenum was in control state and did not change its shape. The collected charge in the ionization chamber for four independent irradiations was corrected by temperature and pressure, multiplied by the detector calibration factor from PTW to get the absorbed dose. Finally, the physical dose was multiplied by the RBE factor, calculated as the mean RBE-weighted dose divided by the mean physical dose within the virtual tumor retrieved from RayStation. Next, control and motion conditions were compared by a two-tailed t-test. The EBT3 films were scanned 24 h after irradiation with an Epson Expression 10000XL (Epson, Japan), using a standardized film scanning procedure (Niroomand-Rad et al 2020, Stengl et al 2023).

3. Results

3.1. Internal structure of PPIeT
The internal disposition of the organs inside the assembled phantom can be seen in the CT images reported in figures 2(A)–(C), along with the CT numbers for the pancreas (48.4 ± 7.5) HU, kidneys (26.58 ± 6.3) HU, and spine (259 ± 18) HU plotted in figure 2(D). For the kidneys, the mean values of the two kidneys were averaged. The CT numbers of PPIeT’s organs present no significant differences compared to human data for the pancreas (54.6 ± 5.8) HU, kidneys (29.5 ± 5.1) HU and spine (203 ± 76) HU. For the superabsorber–water mixture, the measured (2.1 ± 5.8) HU presents no significant difference compared to waters with (0 ± 7) HU.

An illustration of the open PPIeT, with the pancreas, duodenum and two kidneys hanging from the diaphragm lid and the spine remaining inside is shown in figure 3(A). The quantification of the organs’ re-positioning was done by repetitively opening and closing PPIeT’s lid and measuring the deviations from the original position. As reported in figure 3(B), the differences in the mean values of the absolute position in the CC direction were less than 1 mm. The measured differences in the positions are in the range of the MR resolution and the segmentation uncertainty.

3.2. PPIeT’s organs motion: fixed displacements, breathing and GI motion
Pancreas motion of patients was evaluated revealing a range of 0.11 mm up to 19.84 mm with an average value of (5.7 ± 4.6) mm (figure 4(A)). The induced displacements in PPIeT’s pancreas (figure 4(B)) agreed with those of the patients. Linear dependencies from the fixed input displacements were obtained for the pancreas, duodenum and two kidneys in PPIeT (figure 4(C)). The parameters of each linear fit $y = a x + b$ where $x$ is the fixed input displacement and $y$ is the measured displacement, are depicted in table 3. The linear dependency is supported by the obtained $R^2$ values higher than 0.99 for all the organs and makes it possible to obtain a desired
Figure 2. CT images of PPIeT in the coronal plane of the pancreas (A) and kidneys (B). Axial plane with all organs visible (C). The orange arrows indicate the film positions inside the organs in (A), (B) and (C). The measured CT numbers of PPIeT are reported in (D), along with values from literature.

Figure 3. Reproducibility of organ re-positioning. To exchange the detector inserts, the lid of PPIeT was opened and closed (A). Absolute position difference from the original position of each organ during this procedure, where each dot represents an independent measurement (B).
displacement between (3.98 ± 0.36) mm and (18.19 ± 0.44) mm. The \( y \)-intercepts are negative due to a small offset between the actuator and the diaphragm, thus the minimum fixed input amplitude was 10 mm.

The breathing-induced motion of the pancreas and kidneys is reported in figure 5, where it is observed that the organs follow the sinusoidal shape of the input motion. When increasing the input amplitude, an increase in the organs' amplitudes was found with a mean maximum amplitude of (18.02 ± 0.79) mm. The resulting amplitudes of the breathing motion profiles in the pancreas agree with the fixed displacement amplitudes reported in figure 4(C) with mean differences of 0.8 mm, 0.7 mm and 0.2 mm for input amplitudes of 10 mm, 20 mm and 30 mm, respectively. By averaging the results from the three input amplitudes, the pancreas motion yielded a period of (6.9 ± 0.2) s, in accordance with the input period of 7 s.

To simulate GI motion, the duodenum was filled with water and partially emptied, resulting in a shape change. MR images of PPIeT with the full duodenum, considered as the control condition, and the empty duodenum, are reported in figures 6(A)–(D), respectively (for a zoomed-in region). The distance between the duodenum and pancreas yielded an increase from (1.62 ± 0.20) mm to (15.91 ± 0.21) mm for the control and empty state, respectively \((p = 0.0001)\), as plotted in figure 7(A). For further quantification, the outer shape of the duodenum in the axial plane was modeled by an ellipse. The major and minor axes were quantified, and the obtained axis lengths are reported in figure 7(B). Significant differences were obtained for the major axis \((p = 0.0519)\) and the minor axis \((p = 0.0001)\), showing the capabilities of PPIeT to mimic GI motion.

### 3.3. Dosimetric validation of carbon ion dose delivery

To test the feasibility of an end-to-end test using PPIeT, the phantom was irradiated with carbon ions to treat the virtual tumor located at the pancreas head. The treatment plan consists of two beams at different angles, as shown in the planned RBE-weighted dose distribution in figure 8(A). The similarity of PPIeT’s treatment plan compared to two different patients is reported in supplementary figure S3.

First, static irradiation of PPIeT was carried out, yielding a total physical dose of (1.39 ± 0.03) Gy and an RBE-weighted dose of (4.05 ± 0.08) Gy (RBE) in the virtual tumor, for an RBE factor of 2.89. Instead, when breathing motion was applied to PPIeT, lower ionization chamber readings with higher variability were obtained, resulting in a total physical dose of (1.09 ± 0.10) Gy and an RBE-weighted dose of (3.18 ± 0.29) Gy (RBE). A significant difference \((p = 0.0009)\) in the mean values was found (figure 8(B), supplementary figure S4(A)), with an increase in the relative uncertainty from less than 0.04% in the static condition to 8.67% during the breathing motion. The physical dose from every single beam is shown in supplementary figure S4(B).
To further quantify this effect with higher spatial resolution, film dosimetry measurements were done in both static and during breathing motion of PPIeT. Two-dimensional differences between films in static and motion conditions are shown in figure 8(C). The mean profiles from three independent measurements are reported in figure 8(D) for the pancreas and right kidney. Supplementary figure S5 reports raw film data, two-dimensional OD differences of films in static and motion conditions, and mean OD profiles for all the organs. As reported in figure 8(D) for the pancreas, films irradiated during static conditions show reproducibility with a relative uncertainty of at most 1.3%. However, films irradiated during breathing motion show inhomogeneous target irradiation with a relative uncertainty of 5.3%. For the right kidney, a maximum relative uncertainty of 19.0% was found, while for the static condition, the maximum relative uncertainty was 1.1%. For the left kidney, a deviation in the mean value of up to 8.4% comparing static to motion conditions was detected. For the non-
Figure 6. MRI of the full duodenum as control state (A) and of the emptied duodenum (B) in the coronal plane. The pancreas is visible in white and its virtual tumor in black. The orange arrows indicate the measured distance between the pancreas and the duodenum. Zoomed region of the control (C) and empty (D) duodenum (marked by the orange arrows) in the axial plane. The white dashed arrows indicate the length of the major axis (1) and the minor axis (2) in both conditions.

Figure 7. Distance between pancreas and duodenum in control and empty duodenum states (A). Axis length of major and minor axis for control and empty states (B).
moving organs of PPIeT, namely the spine and the spinal cord, films showed mean value deviations lower than 1.5% between static and motion conditions.

4. Discussion

4.1. Phantom setup

PPIeT incorporates anthropomorphic organs of the abdomen that are composed of tissue-equivalent material in terms of their CT contrast. The outer shell of the organs was constructed by 3D printing, which allowed the design and manufacturing of artificial organs with a size and shape resembling human organs. Previous studies have already shown the capability of 3D printing to incorporate customized features in anthropomorphic phantoms (Colvill et al 2020, Halloran et al 2021). This technique enables personalized phantom adaption and easy prototyping. Furthermore, the combination of diverse materials and printing architectures provides a versatile toolkit for achieving different image contrasts or deformability (Colvill et al 2020). For PPIeT, Diran was used as 3D printing material for the spine due to its increased density compared to VeroClear, thus increasing the HU in CT imaging. For the duodenum, a flexible 3D printed material was chosen, making it possible to change duodenal filling independent from breathing motion. So far, the use of flexible 3D printed material for phantoms is scarce. One example is the use of flexible material for artery design (Toepker et al 2013, Filippou and Tsoumpas 2018). However, in most studies, 3D printing material was only used for the molds, which were then filled with silicone or similar flexible materials (Hazelaar et al 2018, Gillmann et al 2021). As shown, when using 3D printing with flexible material, the complex manufacturing steps are streamlined, offering a simplified and more efficient process.
The possibility of detector exchange has already been presented in other anthropomorphic phantoms, and it is an important feature to measure with several detectors since they can have different advantages (Kostiukhina et al 2017, Pallotta et al 2019). Thanks to the versatile process of 3D printing, different inserts can be easily prototyped for the organs such that a straightforward exchange of dosimeters is possible. For instance, in PPIeT, either an ionization chamber insert or film insert can be positioned in the pancreas, and simultaneously film inserts can be positioned in the OARs. In the future, this innovative design can be directly expanded to other detectors without major efforts.

Besides the usage of the versatile technique of 3D printing, the phantom design also incorporates NiDTPA-KCl mixtures to fill the pancreas and kidneys with tissue-equivalent material. With this approach, CT contrast and SPR values match the ones in humans (Elter et al 2022). This method was also used within an anthropomorphic phantom in the publication of Weidner et al (2022). Compared to already published anthropomorphic phantoms, PPIeT uses a superabsorber–water mixture as a filling matrix instead of agarose. Thereby, it is possible to avoid drawbacks resulting from structural breaks of the agarose during motion as well as water collection in these lesions. This can lead to changes in the phantom that are not considered in the treatment plan (Weidner et al 2022). The superabsorber–water mixture has the advantage that it can be physically displaced without harming its structure. It also enables the exchange of dosimeters without destroying the internal matrix, yielding mean differences in the re-positioning of the organs below the MRI resolution.

4.2. Phantom motion

When dealing with pancreatic cancer, it is important to consider the movement of the pancreas and the OARs because this can lead to differences between the planned and delivered doses. A previous study on patients treated with protons showed the robustness of dose coverage for pancreas motion below 3.7 mm (Knäusl et al 2023). Nevertheless, patients’ pancreas movement is not restricted to the margin of the so-called small movers but can increase individually up to several cm in the CC direction (Bhasin et al 2006, Knybel et al 2014, Dolde et al 2019a, Jing et al 2021). To cover this wide range of pancreatic movement observed in patients, breathing-induced motion from 3.98 to 18.19 mm was studied with PPIeT. Smaller displacements were not studied since their influence on dose delivery is expected to be mostly neglectable (Lebbink et al 2022). Since it was possible to linearly correlate the fixed input displacement to the displacement of each organ, any desired organ motion can be achieved. These linear relations made it possible to study the breathing-induced organ motion in PPIeT. Moreover, the lowest amplitude movements achieved in the pancreas and kidneys presented a more precise shape compared to a previous phantom (Weidner et al 2022). Based on the obtained results, it is possible to calculate a desired breathing motion amplitude matching the values of an individual patient.

In addition to the breathing motion, it is important to consider the GI motion, since this can significantly change the dose at the duodenum, one critical OAR in pancreatic cancer treatment (Uchinami et al 2023). A recent study presented a computational phantom that models GI motion in 4D (Subashi et al 2023), but so far and to the best of the authors’ knowledge, there is no anthropomorphic phantom that can simulate GI motion for radiotherapy. PPIeT enables mimicking GI motion by changing the volume of the duodenum, making it possible to study the impact of changes in the distance between the pancreas and duodenum in the course of radiotherapy. The quantitative analysis of this distance change in the phantom matched the results found in patients revealing a relative change from 13.0 up to 18.5 mm (Mostafaei et al 2018). In the future, PPIeT can also be used to study gas accumulation inside the duodenum as this causes dosimetric variations in carbon ion radiotherapy treatments (Kumagai et al 2009).

4.3. Carbon ion treatment of PPIeT

The feasibility of using PPIeT for carbon ion irradiation was tested with a treatment plan equal to that of a patient. Measurements done with the ionization chamber in the pancreas were reproducible within the static condition. A significant reduction in the mean dose value of 21% was observed during breathing-induced motion. The observed difference can have several reasons, one of them being related to the size of the target volume making the ionization chamber partially move out of the beam, especially for the largest input breathing amplitude used. In addition, a larger dispersion in these measurements was obtained, probably caused by dose rate changes, directly influencing the accuracy of the chamber measurements, as reported by Lebbink et al (2022) for carbon ion irradiation during motion. Furthermore, the breathing motion in PPIeT was not synchronized with the beam delivery leading to a possible interplay effect between each single beam spot position and the chamber position (Bert et al 2008, Bert and Durante 2011, Dolde et al 2019b). Additionally, dosimetric films were used in the pancreas and OARs to achieve a high spatial resolution in 2D. Considering that film dosimetry has a limitation related to LET-dependent response (Castriconi et al 2017), the films were positioned facing the beam within their organ position to reduce this effect.
Both, ionization chamber and films, were used to respectively achieve 1D or 2D dose estimations within PPIeT. To extend this to 3D, a possibility would be to use dosimetry gel, a technique that was used in an anthropomorphic phantom with a breathing feature (Mann et al. 2017). However, the irradiation modality used in this study was photons and dosimetry gel presents challenges for carbon ion irradiation due to its LET-dependent response (Maeyama et al. 2023).

In summary, the presented results point towards the need for motion management techniques during carbon ion irradiation for pancreatic cancer. The performance of PPIeT would make it possible to conduct end-to-end tests accounting for breathing motion effects, like gating.

5. Conclusion

To the best of the authors’ knowledge, PPIeT is the first anthropomorphic Pancreas Phantom for Ion-beam Therapy with a breathing and gastrointestinal motion feature for dose QA. PPIeT enables tissue equivalent CT contrast, reproducible positioning of the organs and can simulate the pancreas motion values retrieved from patient data in the range from 4 to 18 mm. The organ motion was achieved for fixed input displacement and sinusoidal breathing motion, following the input period with 99% accuracy. In the gastrointestinal motion study, a mean change of distance between the pancreas and the duodenum of 14 mm was achieved, in accordance with previous patient studies. To assess the influence of the breathing-induced motion in the organs during carbon ion treatment, the developed detector inserts were used. Thereby, an increase of at least one order of magnitude in the dose uncertainty was found during motion conditions compared to static conditions. This is a clinically relevant difference to decide whether carbon ion radiotherapy of pancreatic cancer could be improved by using gating techniques. Overall, PPIeT is a one-of-a-kind tool for dose verifications in the pancreas as well as related organs at risk for precision radiotherapy.

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Data availability statement

The data cannot be made publicly available upon publication because they contain sensitive personal information. The data that support the findings of this study are available upon reasonable request from the authors.

CRediT authorship contribution statement

Christina Stengl: Conceptualization, Methodology, Software, Validation, Formal Analysis, Investigation, Data Curation, Writing—Original Draft, Writing—Review and Editing, Project Administration, Visualization.
Kathrin Panow: Conceptualization, Methodology, Investigation. Eric Arbes: Investigation, Data Curation.

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