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Original Report

Recommendations for MRI-based contouring of gross tumor volume and organs at risk for radiation therapy of pancreatic cancer

H.D. Heerkens MD [a], W.A. Hall MD [b], X.A. Li PhD [b], P. Knechtges MD [c], E. Dalah PhD [b, d], E.S. Paulson PhD [b], C.A.T. van den Berg PhD [a], G.J. Meijer PhD [a], E.J. Koay MD, PhD [e], C.H. Crane MD [e], K. Aitken MD [f], M. van Vulpen MD, PhD [a], B.A. Erickson MD [b,*]

[a]*Department of Radiation Oncology, University Medical Center Utrecht, Utrecht, The Netherlands*
[b]*Department of Radiation Oncology, Medical College of Wisconsin, Milwaukee, Wisconsin*
[c]*Department of Radiology, Medical College of Wisconsin, Milwaukee, Wisconsin*
[d]*Medical Diagnostic Imaging Department, College of Health and Science, University of Sharjah, Sharjah, Dubai*
[e]*Department of Radiation Oncology, MD Anderson Hospital, Houston, Texas*
[f]*Department of Radiation Oncology, Royal Marsden Hospital London, England*

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Abstract

Purpose: Local recurrence is a common and morbid event in patients with unresectable pancreatic adenocarcinoma. A more conformal and targeted radiation dose to the macroscopic tumor in nonmetastatic pancreatic cancer is likely to reduce acute toxicity and improve local control. Optimal soft tissue contrast is required to facilitate delineation of a target and creation of a planning target volume with margin reduction and motion management. Magnetic resonance imaging (MRI) offers considerable advantages in optimizing soft tissue delineation and is an ideal modality for imaging and delineating a gross tumor volume (GTV) within the pancreas, particularly as it relates to conformal radiation planning. Currently, no guidelines have been defined for the delineation of pancreatic tumors for radiation therapy treatment planning. Moreover, abdominal MRI sequences are complex and the anatomy relevant to the radiation oncologist can be challenging. The purpose of this study is to provide recommendations for delineation of GTV and organs at risk (OARs) using MRI and incorporating multiple MRI sequences.

Methods and materials: Five patients with pancreatic cancer and 1 healthy subject were imaged with MRI scans either on 1.5 T or on 3 T magnets in 2 separate institutes. The GTV and OARs were contoured for all patients in a consensus meeting.

Results: An overview of MRI-based anatomy of the GTV and OARs is provided. Practical contouring instructions for the GTV and the OARs with the aid of MRI were developed and included in these recommendations. In addition, practical suggestions for implementation of MRI in pancreatic radiation

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Conflicts of interest: None.

* Corresponding author. Department of Radiation Oncology, Medical College of Wisconsin, 8701 W Watertown Plank Rd, Milwaukee, WI.
E-mail address: berickson@mcw.edu (B.A. Erickson).

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treatment planning are provided.
Conclusions: With this report, we attempt to provide recommendations for MRI-based contouring of pancreatic tumors and OARs. This could lead to better uniformity in defining the GTV and OARs for clinical trials and in radiation therapy treatment planning, with the ultimate goal of improving local control while minimizing morbidity.

Introduction

Pancreatic cancer has an extremely dismal prognosis, with a 5-year overall survival of 5% for all patients.[1] The role of chemoradiation is controversial for both resectable and unresectable pancreatic adenocarcinoma but likely plays an important role for select patients in whom local recurrence is the predominant mode of failure.[2-4]

Radiation dose escalation has been hypothesized to offer an improvement in outcome for patients with locally advanced pancreatic cancer; however, such a benefit remains to be proven in a prospective fashion.[5] Considerable challenges exist in accomplishing dose escalation in pancreatic adenocarcinoma that involve both treatment planning and treatment delivery. Dose escalation for pancreatic head lesions is hampered by the potential for toxicity to the closely positioned duodenum and distal stomach, whereas for body and tail lesions, the more proximal stomach, distal duodenum, and jejunum can be dose-limiting. Accurate tumor contouring as a part of treatment planning is vital as contouring errors are propagated throughout the treatment; therefore, these errors can result in systematic underdosage of the target and/or preventable toxicity to the organs at risk (OARs). Such errors can be considerably consequential when treating patients with dose escalation.

Currently, computed tomography (CT) is the standard for contouring pancreatic tumors for radiation treatment planning. CT offers less soft tissue contrast compared with magnetic resonance imaging (MRI).[6] It has been suggested that MRI can lead to better detection and determination of local tumor extension in pancreatic cancer compared with CT because of its improved soft tissue resolution.[7,8] In addition, MRI has functional imaging capabilities, such as dynamic contrast enhanced MRI and diffusion weighted imaging (DWI). Appropriate incorporation of these data into radiation therapy treatment planning will likely lead to improved targeting of the gross tumor volume (GTV). However, some difficulties can be experienced with MRI (eg, geometric inaccuracies, problems with image registration, motion artifacts). Paulson describes a workflow to integrate MRI simulation in external beam radiation therapy treatment planning, including strategies to manage these challenges.[9] At present, MRI is the standard for contouring tumors in other disease sites such as prostate cancer, spinal metastases, and cervical cancer.[10-12] In line with this, there is a possible role for MRI in contouring of pancreatic cancers and surrounding OARs for radiation therapy planning, especially when dose escalation is to be used.

To our knowledge, no guidelines exist regarding the role of MRI for contouring of pancreatic cancer for radiation treatment planning. The aim of this study is to provide recommendations for contouring of pancreatic cancer using MRI. In addition, our objective is to provide an educational tool to help radiation oncologists routinely integrate MRI into treatment planning, including managing the challenges inherent to MRI.

Methods

The working group consisted of 2 expert radiation oncologists: (BE, WH), a radiologist (PK) and physicist (ED) from the Medical College of Wisconsin (MCW), USA and 1 radiation oncologist (MVV) and 1 radiation oncologist in training (HH) from the University Medical Center Utrecht (UMCU), the Netherlands. In addition to the members of this working group, three radiation oncologists from MD Anderson Cancer Center, USA (EK, CC) and Royal Marsden Hospital London, UK (KA) approved the recommendations.

Patients

The MRI scans of 5 patients with pancreatic cancer and 1 healthy person were used (see also Table 1 for patient characteristics). One healthy person was scanned at MCW on a 3 T diagnostic scanner as part of a screening program for pancreatic cancer. One patient with resectable and 1 patient with unresectable disease were also scanned at MCW in the department of radiation oncology on a 3 T scanner as part of their simulation for radiation therapy planning. The other 3 patients had unresectable pancreatic cancer and were scanned on a 1.5 T scanner in the UMCU as part of their simulation for radiation therapy planning.

MR imaging

This article includes both patients imaged at 1.5 T and 3 T. Both field strengths were included because of variable availability of MRI scanners at different field strengths throughout diverse radiation therapy clinics.

For the UMCU 1.5 T patients, MRI scanning was performed on a 1.5 T Achieva scanner (Philips, Best, The

Netherlands) using a 16-channel phased array torso coil. Patients were positioned with their arms down at their sides, on a diagnostic table top. No alignment with the CT simulation position was performed. Patients wore a custom-manufactured corset to decrease breathing-induced motion of the pancreas. Immediately before scanning, patients drank 300 mL of tap water to increase the contrast between the pancreas and duodenum and stomach. No bowel motion suppression was applied. For respiratory triggered acquisition, a trigger delay of 400 ms was applied after the maximum inspiration to acquire data at expiration.[13]

Postcontrast imaging was performed following intravenous administration of gadobutrol 1 mmol/mL (Bayer Pharma AG, Berlin, Germany) 0.1 mL/kg. This bolus injection was followed by a 20 mL saline flush. A real-time bolus track was performed in the gadolinium contrast procedure. When the contrast bolus was visible at the left side of the heart, patients were instructed to hold their breath at end-expiration.

The MCW patients and healthy volunteer were imaged in the radiation treatment position on a 3.0 T Verio scanner (Siemens Healthcare, Erlangen, Germany) with a custom melamine flat table overlay[9] with arms immobilized above their heads in an alpha cradle. Alignment was performed with the internal bore lasers of the scanner. A combination of the 8-channel spine phased array coil and 2 flexible, 6-channel phased array coils positioned on custom radiofrequency coil bridges were used. Respiratory gating at the end-expiratory phase was performed using pencil-beam navigators positioned at the lung/liver interface. For bowel motion suppression, 0.5 mg glucagon (GlucaGen, Bedford Laboratories, Bedford, OH) injections were administered IV twice, once immediately prior to and once midway through the exam. Postcontrast imaging was performed following administration of 0.1 mmol/kg MultiHance (Bracco, Monroe Township, NJ). Arterial, venous, and portal-venous phase postcontrast images were acquired using breath holds performed at end-expiration.

See Table A in Appendix E1 (available as supplementary material online at www.practicalradon.org) for the scanning parameters of both institutions.

CT imaging

All patients underwent CT simulation to perform dose calculations. The UMCU patients underwent CT scanning on the same day as MRI scanning. The scanning took place 1 week after endoscopic ultrasound guided placement of 4 fiducial markers in the tumor (0.35 × 10 mm Visicoil, IBA Dosimetry, Schwarzenbruck, Germany; or 0.4 × 5 mm gold fiducial marker, QLRAD i\Inc., Miami, FL). The CT protocol consists of a 4-dimensional (4D) CT and a contrast-enhanced CT scan with an arterial and a portal venous phase. Patients were scanned in the treatment position with the custom made abdominal corset.

At MCW, patients underwent 3-dimensional (3D) and 4D CT scanning with oral and intravenous contrast in the treatment position, followed by MRI scanning, either the same day or several days after the CT simulation. No water was given for the MRI scan, but patients were asked to not eat or drink for 4 hours before both the CT and MRI scans.

Registration of images

All images were coregistered to the mid-ventilation position of the 4D CT in the UMCU cases and to the end-exhale position of the 4D CT in the MCW cases. Image registration was performed on the tumor area using rigid, clip box-based alignment in MIM (MIM Maestro, v6.4.3, MIM Software Inc. Cleveland, OH). Manual adjustment of the images was sometimes necessary with priority of alignment with the pancreas rather than the more mobile OARs.

Contouring

The pancreatic tumor was contoured in each of the scans with malignancy present. In the healthy patient, in the absence of a GTV, the different parts of the pancreas were contoured (ie, head and body/tail). The following organs were considered OARs in the treatment of pancreatic cancer: duodenum, stomach, bowel (both including small bowel and colon), kidneys, gallbladder, and liver. Though not contoured for this exercise, the spinal cord and spinal cord plus 5 mm would routinely be contoured for radiation planning. Additionally, the main vessels surrounding the pancreas were contoured for pictorial reasons (celiac axis, superior mesenteric artery [SMA], superior mesenteric vein [SMV], portal vein [PV], inferior vena cava, common hepatic artery, and aorta).

All structures were contoured by all participants of the working group on the MRI scans individually. After delineating all the cases individually, a discussion was held with the radiologist and 3 radiation oncologists (BE, WH, HH) to create the eventual contours of the GTV and OARs. Because the contours are a reflection of the group discussion of the 3 radiation oncologists and the radiologist, no statistical analysis was performed.

Results

Anatomy of the pancreas

The pancreas consists of a head, neck, uncinate process, body, and tail. The head of the pancreas is located in the curvature of the duodenum and is anterior to the inferior vena cava. The most inferior part of the pancreas that is located posterior to the SMV and SMA is called the uncinate process. The neck is a small part of the pancreas between the head and the body, located ventrally to the

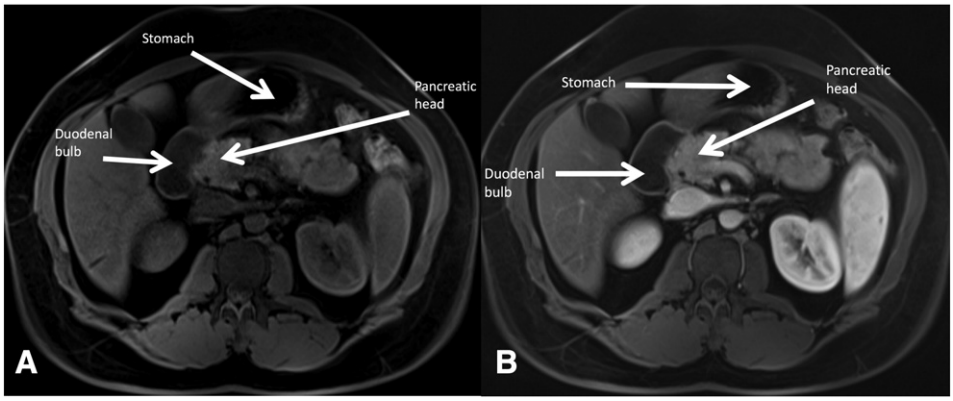

Figure 1 pre contrast T1-weighted image (A) and arterial phase T1-weighted image (B) of the normal pancreas case showing enhancement of the pancreatic tissue and the visibility of the duodenal bulb.

origin of the SMA from the abdominal aorta and where the splenic vein (SV) and SMV join to form the PV. The part of the pancreas located to the left of the midline is called the body of the pancreas. The nomenclature defining the boundaries of the pancreatic tail is not uniform. It has been suggested that the tail is the area where the pancreatic body narrows, or the distal one-quarter of the pancreatic body.

Staging of pancreatic cancer

In pancreatic cancer, prognosis is mainly influenced by the presence or absence of distant metastases and the possibility for resection. In general, 2 systems are used to determine resectability: the National Comprehensive Cancer Network and MD Anderson criteria (see Table B in Appendix E1).[14,15]

Visualization of tumor and OARs

T1-weighted imaging

Normal pancreatic tissue is bright/high signal on T1-weighted imaging (Fig 1). A pancreatic tumor appears as a hypointense or dark area when surrounded by normal pancreatic tissue on T1-weighted imaging (Fig 2, Table 2).[16] In the arterial phase, the tumor enhances to a lesser extent than the benign pancreatic tissue. This phase may also be used to evaluate arterial involvement of the tumor. The later venous phase may show increasing enhancement of the tumor, especially in small tumors. Large tumors and some smaller tumors may remain low in signal intensity. The portal venous phase can be used to assess venous involvement of the tumor and to visualize lymph nodes.[16]

T2-weighted imaging

Pancreatic cancer appears variable on a T2-weighted image.[16] The tumor might be isointense or mildly

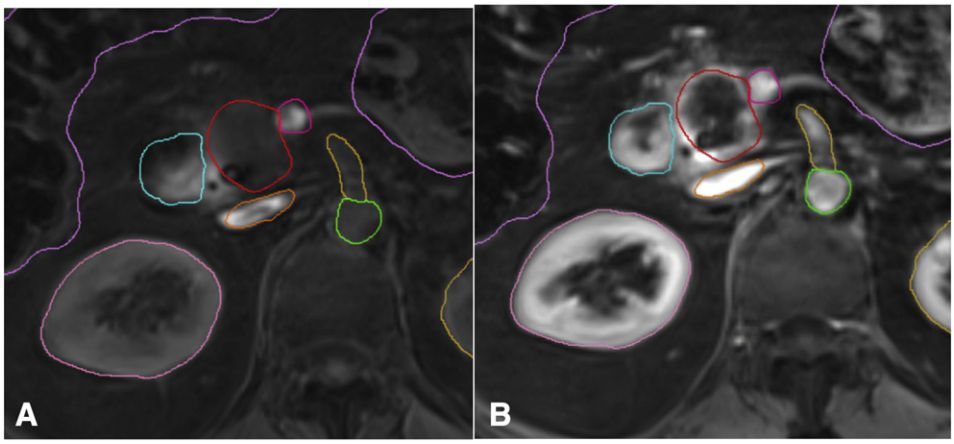

Figure 2 Resectable pancreas case with contouring of tumor and critical structures. Red: GVT, turquoise: duodenum, blue: liver, pink: right kidney, orange: left kidney, bright green: aorta, violet: bowel loops, orange: celiac axis, deep pink: superior mesenteric vein, yellow: portal vein. Note the hypointense area of the GTV on the pre contrast (A) and on the arterial phase (B) images. (Color version of figure is available online.)

Table 1A Three UMCU scanned on 1.5 T MRI

Age (y)	68	71	65
Sex	Male	Male	Male
Tumor location	Head of the pancreas	Body of the pancreas	Body of the pancreas
Encasement of vessels	Occlusion of SMV, SV; 360° encasement of SMA, GDA	360° encasement of CA, HA, LGA; 90° abutment of PV; 90–180° abutment of SMV	360° encasement of CA, SA, HA; 90° abutment of SV; 90–180° abutment of PV
Resectability	Unresectable	Unresectable	Unresectable
Stent in CBD	Plastic stent	None	Metallic stent
Prior chemotherapy	None	None	None

hypointense compared with the surrounding pancreatic tissue. It is therefore difficult to define the borders of the GTV with this sequence; however, T2-weighted images create an excellent contrast for visualization of the pancreatic and common bile ducts. This might help define the extent of the tumor in the pancreas itself as a result of pancreatic duct disruption or common bile duct obstruction in association with pancreatic tumors (Fig 3). Cystic areas in close vicinity of the tumor can be demarcated on T2-weighted images (Fig 3). Figure 4 illustrates the presence of an abrupt ending of the visualized pancreatic duct and clear demarcation of GTV.

Diffusion-weighted imaging

In DWI, the random Brownian motion of water molecules is depicted and reflects tissue cellularity. Cancer-containing tissue is more cellular than noncancer tissue and restricts the diffusion of water. In the majority of patients, a pancreatic tumor appears as an area with increased diffusion restriction (Fig 5).[17] In the literature, a sensitivity of 0.86 (95% confidence interval, 0.78–0.91) with a specificity of 0.91 (95% confidence interval, 0.81–0.96) for detecting pancreatic cancer with DWI was found.[18] However, discriminating pancreatic cancer from pancreatitis or healthy pancreatic tissue with DWI is difficult. Areas of restricted diffusion can be used to locate areas of pathology but should not be used for contouring. Both pathologic and benign lymph nodes show diffusion restriction with DWI.[19] Therefore, DWI is not suitable for assessment of pathologic lymphadenopathy.

Practical recommendations for contouring

MRI requirements

To integrate MRI in radiation therapy treatment planning, several requirements must be met. To overcome registration issues, patients are best imaged in the radiation therapy treatment position on the same day as CT simulation and with reproducible filling of OARs, such as the stomach and duodenum. Restricting eating and drinking for 2 to 4 hours before simulation and daily treatment may aid in minimizing variable gut distention. Administration of glucagon can be considered to minimize the peristaltic motion of the gastrointestinal tract.

To facilitate registration between CT simulation and MRI simulation, and between treatment planning and during treatment, motion management strategies are best chosen in advance. In this way, CT and MRI scanning can be performed in the same respiration phase to create fewer registration issues. Manual adjustment of the registration is usually needed with priority placed on aligning tumor-bearing tissues rather than the adjacent organs at risk. Differences in organ filling and patient positioning should be minimized to improve the registration.

In addition to motion management during scanning, the insertion of fiducial markers can facilitate registration between the CT and MRI. Furthermore, it allows for highly accurate image guided radiation therapy. The choice of fiducial marker type is dependent on the clinical purpose. Visibility of these markers is best achieved with iron-based markers; however, these might induce artifacts on DWI. If distortions of the DWI are to be avoided, then noniron markers are preferred.[20]

Table 1B Three MCW patients scanned on 3 T MRI

Age (y)	20	80	65
Sex	Male	Male	Male
Tumor location	NA	Head of the pancreas	Body of the pancreas
Encasement of vessels	NA	90° abutment of SMV	360° encasement of CA, HA, and LGA, and of SV, SMV and PV; 180° abutment of the SMA and aorta and involvement of the left adrenal gland
Resectability	NA	Borderline resectable	Unresectable
Stent in CBD	NA	Metallic stent	No
Prior chemotherapy	None	None	Yes: 8 cycles of FOLFIRINOX

CA, celiac axis; GDA, gastroduodenal artery; HA, hepatic artery; LGA, left gastric artery; NA, not applicable; PV, portal vein; SA, splenic artery; SMA, superior mesenteric artery; SMV, superior mesenteric vein; SV, splenic vein.

Table 2 Visibility of GTV and organs at risk with different scanning sequences and contouring

Sequence	Visibility of	Needed for
T1 W	Normal pancreas is bright Tumor area is hypointense	Tumor contouring
T2 W	Normal pancreas, pancreatic duct, cysts Duodenum and stomach Other critical structures (small bowel, colon, liver, kidneys, spinal chord	Distinguishing normal pancreas from tumor Distinguishing tumor from duodenum and stomach Contouring of critical structures
Contrast enhanced		
Arterial	Tumor as a hypointense area, normal pancreas as a hyperintense area	Tumor discrimination from surrounding pancreas
Venous	Venous structures	Contouring of venous structures Tumor discrimination from surrounding pancreas
Delayed venous phase	Portal vein	Contouring of portal vein
DWI		
Low b-values	Anatomy	Registration to other sequences
High b-values	Diffusion restriction in tumor, lymph nodes (both pathologic and non-pathologic), bowel areas	As this sequence is very sensitive, although not specific, and geometric inaccuracies may exist, careful use of this sequence.
ADC		Differentiation of restricted diffusion from T2 shine through

T2W: T2-weighted imaging, T1W: T1.

The choice of field strength implies different pros and cons. For higher field strengths (ie, 3 T), higher susceptibility effects, and thus increased geometric distortions, will be present. In addition, motion artifacts are more pronounced. In lower field strengths (ie, 1.5 T), scan times will be prolonged to reach similar contrast to noise ratios as at 3 T; therefore, no definite conclusion can be drawn as to which field strength is optimal.[9]

In concordance with CT simulation, a slice thickness of ≤3 mm is advised for MRI simulation when contouring the GTV and geometric distortions must be less than 2 mm.[9]

GTV

It is advised to contour the GTV in conjunction with, or after discussion with, an experienced radiologist.[21] To start contouring, the T1-weighted sequence without intravenous gadolinium is used and the hypointense or dark area is included in the GTV (Fig 6). Subsequently, the T1 series with intravenous gadolinium are used to confirm or optimize the GTV. When in doubt about areas of involvement with tumor, the high b-value DWI might help in localizing and contouring the GTV (Fig 7). However, the sensitivity of DWI concerning the primary tumor is high; nevertheless, the specificity of areas with diffusion restriction is low. DWI can be prone to geometric distortion. Further, restricted diffusion can be confounded by T2 shine through; therefore, we suggest looking at the high b-value DWI images and corresponding apparent diffusion coefficient maps after finishing contouring of the GTV on the T1-weighted images to evaluate areas of contradiction.

Pancreatic cancer is sometimes associated with cysts. Because invasive carcinoma is almost always present in

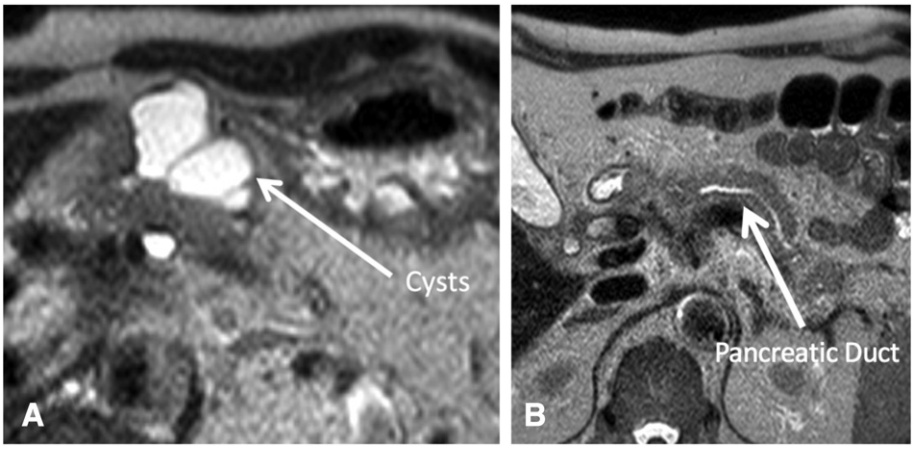

Figure 3 A: Visualization of cystic areas (A) and pancreatic duct (B) on T2-weighted imaging at 1.5 T.

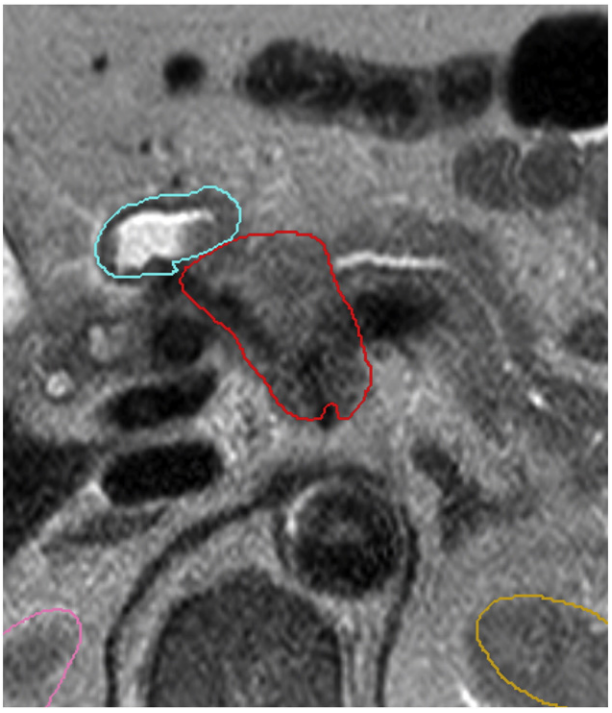

Figure 4 T2-weighted image, an example of gross tumor volume in red and duodenum in turquoise. (Color version of figure is available online.)

these cyst walls, it would be best to include them in the GTV if the dose to the OARs allows for this. However, such cysts can be quite large, and it should be left to the clinical discretion of the radiation oncologist as to whether such cysts can be safely included within the GTV without creating a prohibitively large GTV.

OARs

The OARs are best seen on the T2-weighted images, whereas the GTV is best seen on the T1-weighted images. This can lead to issues with alignment of the GTV and the OARs. The stomach can be contoured on the T1-weighted images to prevent problems with registration. The T2-weighted images can help if there are areas of doubt. The stomach has to be contoured from the esophageal junction up to the pylorus. Contouring of the duodenum should be performed from the pylorus up to the ligament of Treitz and, when visible, can be performed on the T1-weighted images. Also, the areas of duodenal invasion, as seen on the T2-weighted images, need to be included in the GTV.

In pancreatic cancer, it is common to contour the individual small and large bowel loops. However, creation of a "bowel region" or "bowel bag" is also a possible solution, especially because it can be difficult to accurately separate the small and large bowel in some patients. This consists of the peritoneal contents after subtracting the planning target volume, stomach, duodenum, and other OARs.[22] Both strategies have their own dose constraints and dose-volume histograms. As long as the appropriate dose constraints are used, both can be applied. For an example of OAR contouring, see Fig 8.

Contouring of vessels is best performed on arterial and venous phases of the contrast-enhanced T1-weighted images. Awareness of the anatomical location of these vessels is important because these structures can potentially be used for creating elective nodal clinical target volumes. CT-based contouring of vessels for this purpose has been previously described by Goodman et al. and Jabbour et al.[23,24] Additionally, contouring of these major arterial trunks can also be used to cover areas of occult perineural spread of pancreas cancer.

Discussion

Integrating MRI into radiation treatment planning for pancreatic cancer can lead to more accurate target definition. Combining this treatment planning technique with MRI-based image guidance is expected to lead to a smaller planning target volume margin as compared with CT and reduce the dose to normal tissues. This might enhance the ability to escalate dose to the pancreatic tumor and thereby increase local control rates without increasing toxicity.

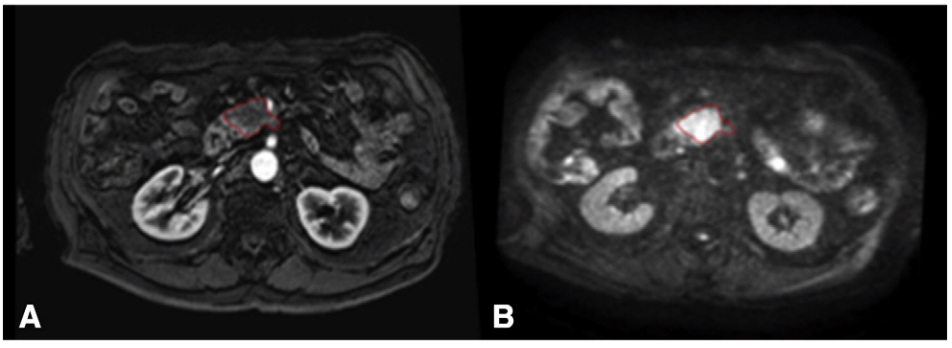

Figure 5 Unresectable pancreas case with contouring of tumor on arterial T1-weighted image (A) and on DWI (B). Red line: GVT. Note the hypointense area on the T1-weighted image and the diffusion restriction on the DWI. (Color version of figure is available online.)

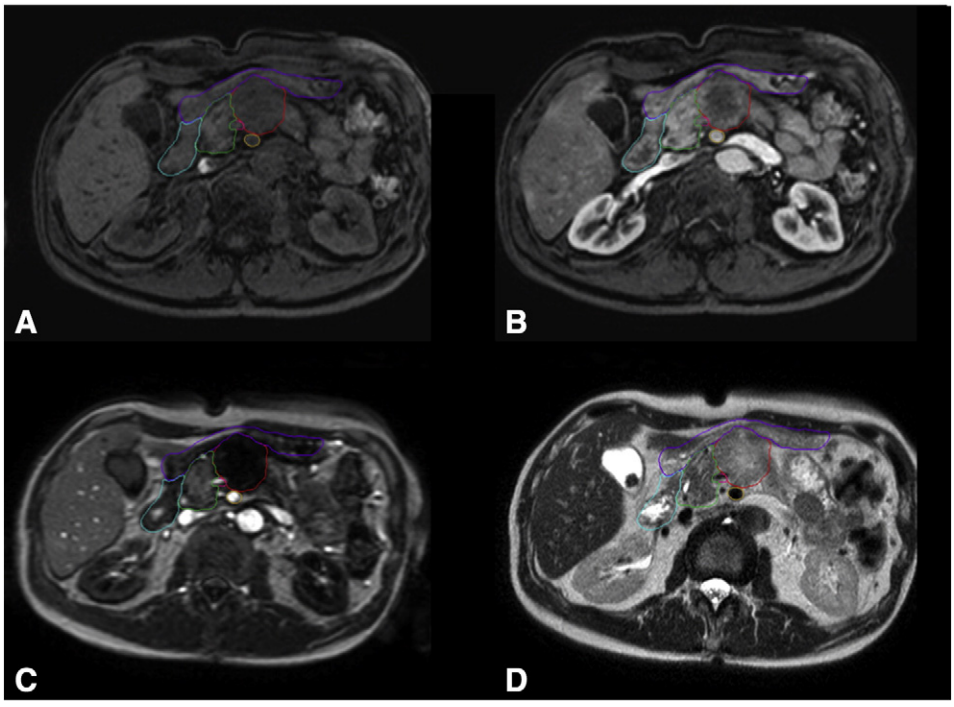

Figure 6 Contouring of an unresectable pancreatic tumor in the pancreatic body on pre contrast T1-weighted (A), arterial T1-weighted (B), T1-weighted (C), T2-weighted (D). Red: GVT, turquoise: duodenum, dark green: pancreatic head, purple: stomach. (Color version of figure is available online.)

This study describes recommendations for contouring pancreatic tumors and OAR with the aid of MRI. The recommendations are based on both 1.5 and 3 T images and 2 different scanning protocols. Even though there are differences, contouring of the GTV and OARs has been shown to be possible with both techniques. The registration of the data sets was somewhat more difficult for the UMCU patients because there were rotational differences resulting from lack of immobilization. This had no consequences for the GTV contouring; however, for contouring of OARs, the registration errors were larger, especially when located farther away from the GTV. This shows the need for MRI scans in the treatment position. Although the MCW patients were scanned in their treatment position, image coregistration could be challenged by differences in internal anatomy because of CT and MRI scans being acquired on different days.

In cases in which dose escalation is being considered, we suggest patients undergo MRI simulation because it can be very helpful in defining the tumor and OARs at the time of contouring. As shown, the tumor can best be visualized and contoured with the arterial phase T1-weighted images. The high b-value DWI can also be helpful to define tumor extension. Visualization of the duodenum and the stomach is best performed with T2-weighted imaging, but use of the T1 images is also possible so that the contours of the GTV and the stomach and duodenum will be properly registered.

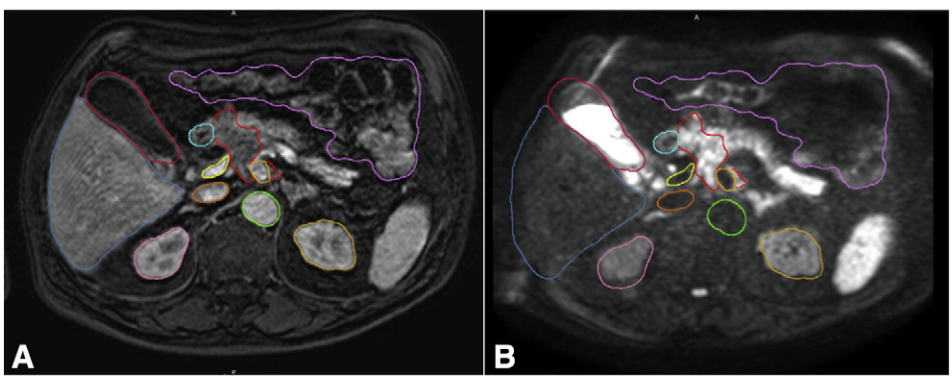

Figure 7 Contouring of an unresectable pancreatic tumor in the pancreatic head on arterial T1-weighted (A), and DWI (b-value 800 s/mm^2) (B). Red: GTV, turquoise: duodenum, blue: liver, pink: right kidney, orange: left kidney, red: gall bladder, bright green: aorta, violet: bowel loops, orange: celiac axis, yellow: portal vein, red-orange: inferior vena cava. (Color version of figure is available online.)

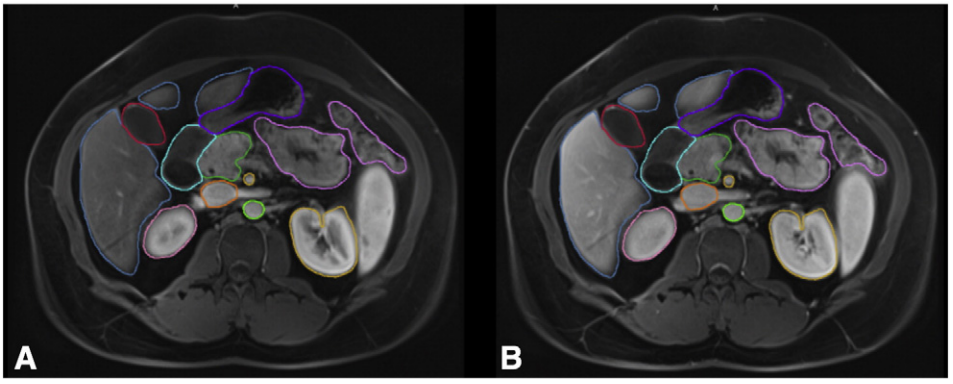

Figure 8 Normal pancreas case with contouring of pancreas and critical structures on T1-weighted image, precontrast (A) and arterial phase (B). Dark green: pancreatic head, turquoise: duodenum, purple: stomach, blue: liver, pink: right kidney, orange: left kidney, bright green: aorta, violet: bowel, orange: celiac axis. (Color version of figure is available online.)

One of the major limitations of this study is the lack of pathology correlation with the imaging contours. Pathologic correlation is the foundation for determining tumor extension. Up to now, no voxel-wise comparison between MRI and pathologic specimens in pancreatic cancer has been performed. A comparison of the largest tumor diameter measured with MRI and pathologic specimens after resection has previously been performed. This showed an underestimation of the tumor diameter by 4 mm.[25] Also in the CT studies, a discrepancy between tumor size and the pathology specimen was found. In 1 study, tumors with an average size on pathology of 34 mm were underestimated with CT by 7 mm.[26] In another study, no significant difference between 3D–CT and pathology tumor diameters was found.[27] However, there was a wide range of the degree of radiologic-pathologic discrepancies. Tumors larger than 3 cm were underestimated on 3D–CT by 8 mm, whereas tumors <3 cm were overestimated by 4.2 mm. Previous research by Dalah et al investigated the maximum tumor diameter of the pathology specimen, compared with partly automated delineation of the GTV with positron emission tomography, MRI, and CT.[28] They showed that there is no apparent consensus about the optimal imaging strategy for defining the GTV. No evidence for the additional value of FDG-positron emission tomography in delineation of pancreatic tumors currently exists.[29]

Future studies with voxel-wise comparison of pathologic specimens and MRI have to provide insight into the correlation between tumor properties and MRI features. This might imply a reduction of contouring uncertainties.

In general, there are some difficulties with the use of MRI for radiation therapy planning for pancreatic tumors. First, registration between different MRI sequences and the CT simulation can be difficult because of geometrical changes of the OARs.[28] These image registration errors can be avoided by using a single imaging modality, and, whenever possible, use of the T1-weighted MRI sequence. In spite of this, CT is currently still needed for dose calculations in present radiation therapy practice. With recent developments in MRI-based treatment planning, there could be a time in the future when MRI-only treatment planning in pancreatic cancer is a reality.[30] The anatomical location of the stomach and duodenum changes over time, especially because of filling differences and contractility of these organs. Our suggestion is to implement an OAR filling protocol and perform MRI simulation in the treatment position to minimize the possibility of geometrical changes. In addition, we prefer to perform registration of the different sequences based on the tumor area, or, if available, on intratumoral fiducial markers, that are visible both on MRI and CT scans. This technique will allow for the most accurate GTV contouring. In addition, contouring of the adjacent OARs on the same sequence (T1) is the most accurate. This is exceedingly important because the adjacent OARs are in the high dose area and must be accurately defined.

Second, at times there are discrepancies between tumor areas as depicted on CT and MRI scans or on different MRI sequences. Use of only 1 imaging modality for treatment planning, preferably MRI, will reduce these errors.

Third, geometrical distortions are mainly seen in DWI when acquired using conventional single-shot echo-planar imaging sequences. Optimization of sequence parameters, scanning at lower field strengths, and application of correction algorithms during reconstruction using magnetic field maps acquired during the MRI examination can diminish the severity of geometric distortions in DWI.[15]

In addition, there are more drawbacks to the use of MRI in radiation therapy treatment planning. These include the cost of MRI in addition to a CT scan, patient discomfort, and the extra time required for fusing and contouring. Because we think that the superior soft tissue contrast of an MRI scan might lead to improved contouring of pancreatic tumors and OARs, higher doses might be possible with smaller margins. This might lead to better outcomes and could outweigh the drawbacks of adding MRI scans to radiation therapy treatment planning.

One of the future directions for the application of MRI in radiation therapy for pancreatic cancer is adaptive radiation

therapy. Next to better soft tissue contrast, spatially heterogeneous biological properties of tumors can also be revealed with MRI scans. This allows dose painting (eg, selective dose escalation). In addition, MRI-based response assessment during treatment might lead to adjustment of the treatment plan as a result of biological changes of the tumor. This has been preliminarily shown in rectal and esophageal cancer with DWI acting as an imaging biomarker.[31,32] Individualized treatment can eventually prevent under- or overtreatment. MRI also allows for response assessment during treatment, which may be prognostic. This might lead to better patient selection for dose escalation before treatment is completed. Finally, the superior soft tissue contrast may allow more accurate image registration during image guided treatment.

In addition to showing the biological properties of pancreatic tumors, MRI scans can provide insight into pancreatic tumor motion in the form of cine MRI or 4D MRI.[13,33,34] This can be used as tool to choose motion management strategies and individualized treatment margins.

In conclusion, MRI holds promise for radiation planning and delivery for pancreatic cancer. In this article, we have provided insight into the use of MRI in contouring of pancreatic tumors and OARs. This can be extended to individualizing radiation therapy treatment based on biologic markers and response, and individualizing treatment margins by motion characterization. For dose escalation patients, the essentials include respiratory motion management, no water or food status before treatment, MRI simulation in the treatment position, and daily image guidance with good soft tissue delineation.

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