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ORIGINAL ARTICLE

An innovative strategy for the identification and 3D reconstruction of pancreatic cancer from CT images

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Abstract We propose an innovative tool for Pancreatic Ductal AdenoCarcinoma 3D reconstruction from Multi-Detector-Computed Tomography. The tumor mass is discriminated from health tissue, and the resulting segmentation labels are rendered preserving information on different hypodensity levels. The final 3D virtual model includes also pancreas and main peri-pancreatic vessels, and it is suitable for 3D printing. We performed a preliminary evaluation of the tool effectiveness presenting ten cases of Pancreatic Ductal AdenoCarcinoma processed with the tool to an expert radiologist who can correct the result of the discrimination. In seven of ten cases, the 3D reconstruction is accepted without any modification, while in three cases, only 1.88, 5.13, and 5.70 %, respectively, of the segmentation labels are modified, preliminary proving the high effectiveness of the tool.

Keywords Pancreatic ductal adenocarcinoma · Image segmentation · 3D reconstruction · 3D printing

Introduction

Pancreatic cancer accounts for about 3 % of all cancers and about 7 % of cancer deaths in the United States, where in 2016 are estimated to be noticed 53,070 new cases, and 41,780 death both in male and female [1–3]. Pancreatic cancer survival has not improved substantially over the past 30 years, with most patients dying within 5 years because of cancer-related complications [3, 4]. Men are 30 % more affected than women, and incidence rate is 50 % higher among Blacks than Whites and people of other races [2]. Carcinoma of the exocrine pancreas accounts for over 90 % of pancreatic tumors [5]: among these, 95 % are of Pancreatic Ductal AdenoCarcinoma (PDAC) type [2].

At the present state, surgical resection represents the only curative treatment, but at presentation, only 10–15 % of patients with pancreatic cancer are considered surgically resectable [6]. For patients with advanced disease, only palliative therapies are possible. Multi-Detector-Computed Tomography (MDCT) is referred as the gold standard among imaging techniques for pancreatic cancer detection and staging: a venous medium contrast is used to obtain a better tumor mass visibility and PDAC usually appears as a hypodense area. One of the main limits of MDCT technology is that only vascularized tumor area, that is the inner one, looks hypodense, and hypodensity decreases from the center to the boundary of the tumor. Thus, with respect to other abdominal organs tumors, PDAC is characterized by a particular shaded appearance that makes very hard a clear identification of tumor borders.

Decision making on patient operability is a challenging task, and PDAC resections are regarded as among the most complex abdominal operations. Thus, both patient operability and surgical planning must be carefully evaluated. Patient's evaluation commonly relies only on MDCT images and radiologic reports in the daily practice, and no specific visualization technologies are available to help the surgeon in the decision making and the surgical planning.

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Methods

The first step of the process is a semiautomatic segmentation of the pancreatic parenchyma and all the other structures of surgical interest. Segmentation is performed using the open-source software ITK-Snap [7, 8] and a specific tool derived from it, the Endocas Segmentation Pipeline (ESP) [9]. This segmentation tool is studied to face main problems in pancreas segmentation. In fact, pancreas is in close contact to other abdominal structures and cannot be easily distinguished from them because of great similarity within their Hounsfield Units (HU)s, a quantitative scale for describing radiodensity [10]. Segmentation is the process of partitioning an image into different regions, homogeneous for some characteristics of interest. Segmentation should stop when the object of interest is isolated [11].

ESP approach is based on a specific segmentation sequence, in which each structure is segmented in its best-enhanced contrast phase and then removed from the MDCT data set. According to the required information for the intervention planning, we include into the virtual model, peri-pancreatic arteries and veins, biliar and Wirsung duct, and part of the duodenum. Pancreas is the last organ to be segmented, to have no other structures close to it. Segmentation is performed through a region-growing algorithm with a homogeneity function that takes into account the intensity of the neighborhood voxels—neighborhood connected region growing—and the maximum curvature allowed to the boundaries of the segmentation surface—it can be force to a smooth surface or it can shape into fine details—[9].

PDAC Discrimination Algorithm

Since standard available algorithms are not suitable to approach PDAC segmentation, we propose a tailored routine, developed in Matlab® (R2007b, the Math Works, Natick, MA) environment [12]. The tool works on MDCT pancreatic or arterial phase data set, where we have the highest contrast between tumor and parenchyma and carries out the discrimination between health and tumor tissue using a fuzzy logic system [13–15]. Fuzzy logic has been preferred to other classification algorithms because it:

- allows the construction of flexible systems;
- is an intuitive approach, based on simple mathematical concepts;
- can be built on the experience of experts, in our case radiologists;
- is tolerant of imprecise data.

The last feature is particularly important to analyze even noise affected MDCT. Furthermore, simple mathematical concepts simplify the interaction with medical field experts. A Fuzzy Inference System (FIS) is a system that carries out an input–output mapping based on fuzzy logic. System output depends on implemented Membership Functions (MF)s and user-defined rules.

In our case, the system takes as an input each image pixel of each MDCT slice, and returns its probability of being part of the tumor mass. The discrimination process is carried out using the following criteria:

- Pixel similarity to the gray level of the tumor mass center;
- Pixel similarity to the health tissue gray level;
- Average of pixel 3×3 neighborhood to the gray level of tumor mass center.

The last criterion has been introduced to eliminate pixels with a tumor-like gray level, but not belonging to the tumor mass. To retrieve the three above-mentioned characteristics from images, we implemented an interactive procedure: the user can simply select a gray level that is highly representative of the tumor as well as a value representative of the health tissue, directly on images. These values are used to initialize MFs and build the system. This is a crucial point to allow the system to adapt to different image data sets and to not be affected by changes in tissue densities. Each characteristic of interest is represented by three fuzzy sets, describing three different similarity levels through proper functions. The discrimination FIS analyses each image pixel, giving in output its probability of belonging to the tumor. The output ranges between 0 and 1, where 0 denotes a pixel certainly coming from the health tissue, and 1 refers to a pixel that surely belongs to the tumor. This new image re-mapping is used as a guide for a region-growing algorithm with the same characteristics of the one implemented in the ITK-Snap software and applied for abdominal structures. Through a proper interface, the user selects the starting point of the algorithm, as close as possible to the tumor mass center. Unlike the ITK-Snap segmentation algorithm, here, the evolution of the algorithm ends automatically. The result of the region-growing algorithm is used to isolate the tumor region from the background, to create a segmentation label set useful for the 3D rendering. Finally, we discretize the gray-scale colormap into five levels, one for health tissue and four describing different tumor hypodensity levels (see Fig. 1). The darkest labels represent the highest confidence in tumor identification, while the lighter the lowest. As a final step, the segmentation label set for the tumor is merged with the one of previously obtained for abdominal structures, to get a unique set suitable for visualization and 3D rendering in the ITK-Snap software, as depicted in Fig. 2.

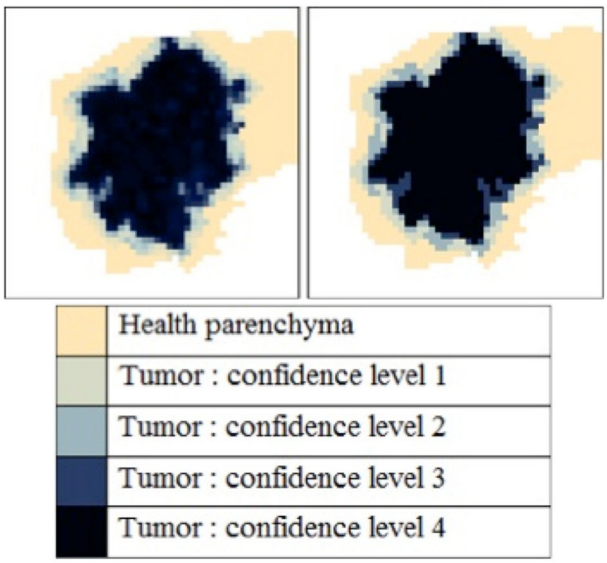

Fig. 1 Full scale (*left*) and discretized (*right*) colormap in 5 levels. A description of thecolormap (*bottom*) where Level 1 represents the lowest confidence in tumor

Preliminary assessment

To evaluate the performances of the developed tool, we analyzed ten cases coming from the Radiology Department of Karolinska Institutet (Stockholm, SE) relating PDAC cases occurred at the head of the pancreas, with different grades of Superior Mesenteric Vein (SMV) or Superior Mesenteric Artery (SMA) involvement. Images were acquired with venous contrast medium injection, and each data set includes arterial, pancreatic, and portal-venous contrast phases. Images were acquired using a Siemens 64-slice MDCT, and reconstructed using a slice thickness ranging from 0.6 to 2.5 mm. Each case has been processed using the ITK-Snap software with ESP to perform the segmentation of the main abdominal structures, following the order reported here below:

1. aorta and main peri-pancreatic arteries;
2. portal vein and its main branches;
3. inferior vena cava;

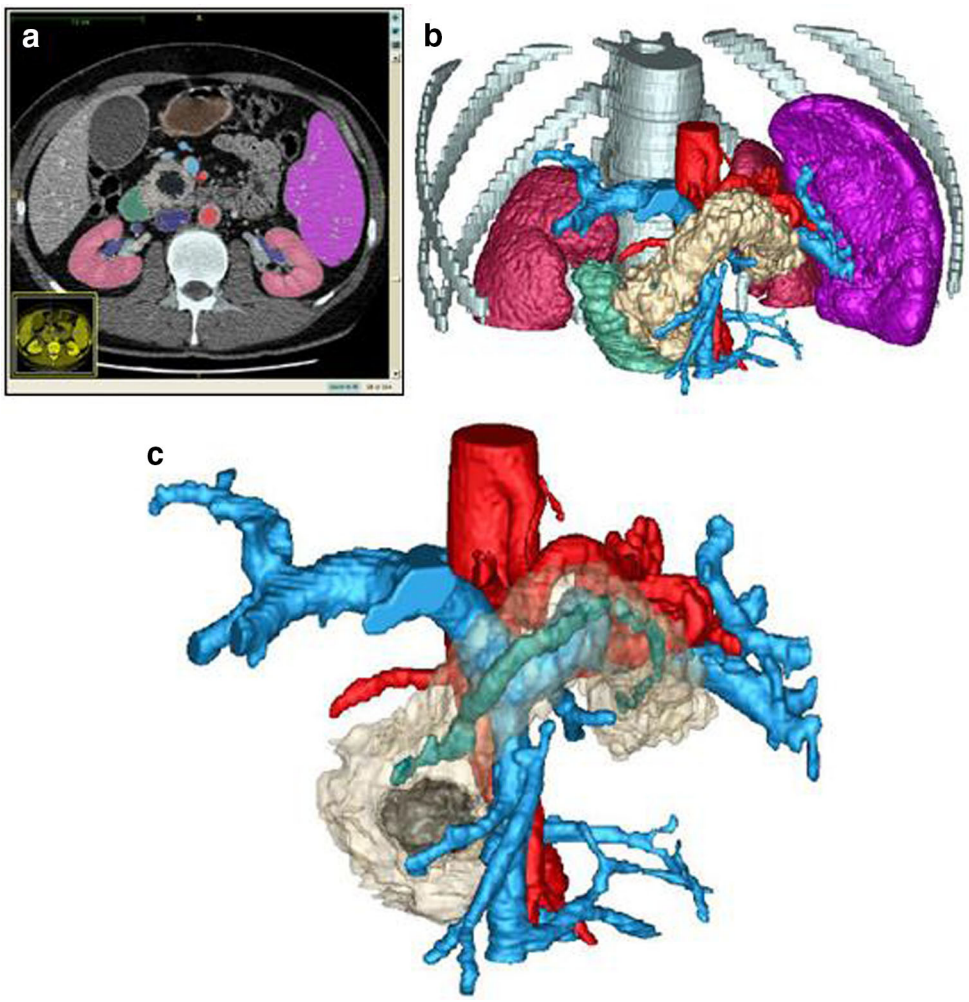

Fig. 2 Final label set (**a**) and 3D rendering (**b**, **c**) for a PDAC case study

Table 1 Details of the amount of corrections applied to the 3 modified label sets: structures in contact with the tumor, types of error and

# MDCT	Infiltration	Corrections	Overall differences (%)
1–7	SMV and/or SMA	–	0.0
8	SMV	Interface between SMV and tumor not completely identified	1.88
9	SMV + SMA	Tumor over-estimation at the interface with duodenum	5.13
10	SMV + SMA	Tumor over-estimation at the interface with duodenum + intra-peritoneal fat identified as tumor	5.70

4. gallbladder and biliar ducts;
5. Wirsung duct;
6. second and third parts of duodenum;
7. biliar stent, if present.

Then, we applied the developed tool to segment the tumor mass. We presented the resulting segmentation labels and the 3D rendering to a radiologist with a deep expertise in PDAC assessment, using the ITK-Snap software. The radiologist could navigate through axial, coronal, and sagittal views of the resulting label set superimposed to the original MDCT slices, along with a 3D rendering of the model. The radiologist was allowed to manually correct each tumor label, according to his experience.

Results

To carry out a quantitative comparison, we developed a Matlab® routine to compute differences between the tumor label set provided by our tool and the one checked by the radiologist. The comparison routine works slice per slice on the original and the corrected label set and compute the differences between the two sets for each label, expressed as a percentage of the total covered area. In seven of ten cases, the radiologist did not make any modification and completely approved the model: a complete approval means that the model contains all the information of interest for the surgeon to assess patient operability and eventually plan the intervention. In the other three cases, the radiologist made slight modifications to the models, summarized in Table 1. Segmentation results can be highly affected by the quality of MDCT images, especially in terms of tumor enhancement and accuracy of the timing of different contrast phases. This factor must be taken into account in the evaluation of tool results. MDCT quality evaluation has been done in a qualitative way, relying on the experience of the radiologist in identifying a good MDCT scan with respect to the correct timing of contrast phases, the noise level of the data set, and the level of enhancement of the tumor. The latter one, of course, could be not linked only to the quality of the MDCT, but also to the specific features of the tumor (Table 2). Fig. 3 depicted

Table 2 Classification of the quality of MDCT scans in terms of tumor enhancement, phases timing correctness, image noise

# MDCT	Tumor enhancement	Timing	Noise
1–7	Good	Good	Very low
8	Good	Good	High
9	Poor	Good	Low
10	Poor	Poor	Very low

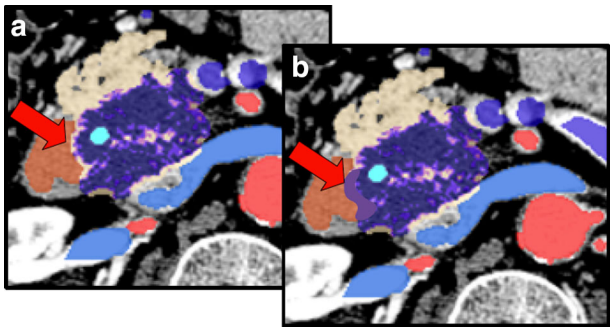

Fig. 3 PDAC label set before (**a**) and after (**b**) radiologist corrections: the *red arrow* indicates the tumor-duodenum interface correction

an MDCT slice before and after radiologist correction. As regard the SMV interface, errors come from an incorrect inclusion during the application of the region-growing algorithm, while it was correctly identified during the fuzzy discrimination. As regard tumor–duodenum interface, the main problems concern the high similarity in terms of HUs of the two structures. During fuzzy discrimination between health and tumor tissue, pixel belonging to duodenum is classified with a low probability of belonging to the tumor and then included into the tumor mass through the region-growing algorithm.

Discussion

The literature shows few works related to pancreas segmentation procedures [16–21] or multi-organ segmentation procedures including also the pancreas [22–24], with exception of ESP [9]. In fact, it is a not trivial task, due to the poor contrast of the pancreas with respect to the

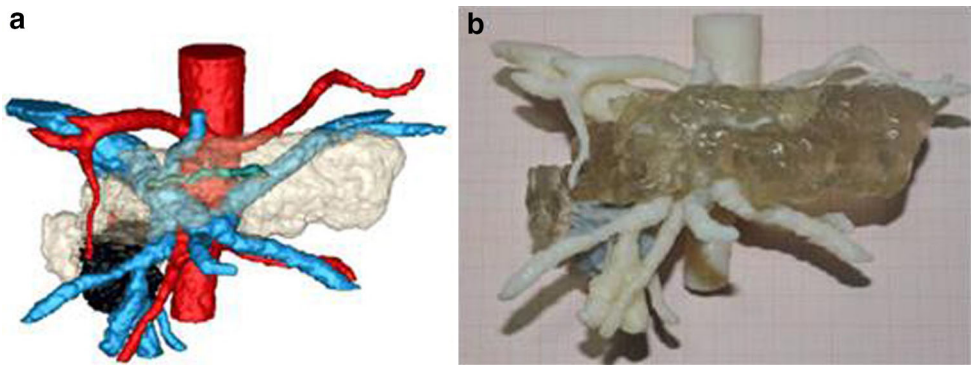

Fig. 4 Virtual (*left*) and 3D printed (*right*) pancreas model

surrounding structures. The identification and 3D reconstruction of pancreatic tumors, such as PDAC, are not faced in none of these works.

ITK-Snap and ESP, with respect to other available works, are based on simple mathematical concepts, and they are easy to use for people without a deep scientific preparation. The proposed solution follows the aim of simplicity of use that characterizes ITK-Snap. A semiautomatic solution has been preferred to a completely automatic one, due to the negligible difference in HUs between tumor and health tissue and their significant variability in terms of HUs among patients. Thus, a completely automatic solution would be less reliable in the correct identification of the tumor, while a semiautomatic one results more robust and widely applicable. The use of a probability map to describe the tumor morphology allows preserving an informative description of tumor borders. Actually, PDAC tumor visibility on MDCT images is quite poor and characterized by unclear borders, with respect to other types of pancreatic and, more in general, abdominal tumors.

Starting from the ESP result, our algorithm provides tumor segmentation and a new resulting label set in few minutes, with a little and easy user interaction. These features are crucial to encourage the integration of virtual 3D reconstruction techniques into clinical daily practice.

The time required for the radiologist to completely correct a label set ranges between 15 and 40 min depending on the amount of modifications. This time will be significantly reduced introducing some facilities aimed at making easier the radiologist interaction with segmentation labels: in particular, we will resample segmentation labels to fit a 5 mm slice thickness, commonly used by radiologists during MDCT evaluation. At the present state, modification was carried out on MDCT reconstructed at a slice thickness ranging from 0.6 to 2.5 mm, thus lengthening a lot the interaction time.

The cases totally approved by the radiologist were rated as the best quality images in terms of tumor enhancement: thus, to get the best results from the developed tool, a defined acquisition protocol should be adopted. In particular, arterial, pancreatic, and portal-venous phases must be always available, and the duodenum should be dilated using carbonated powder to simplify its segmentation, relying on the air contained in it. Moreover, the breath synchronization of all the different contrast phases would be fundamental to avoid misalignments.

The assessment of the tool effectiveness is currently limited to the radiologist evaluation: this limit will be overcome through a further investigation based on the quantitative comparison between the tumor label set resulting from the segmentation and the surgical specimen, analyzed by an expert pathologist.

The virtual 3D model allows a detailed analysis of tumor location, morphology, and hypodensity levels, and related to peri-pancreatic vessels and other abdominal structures. Despite all this interesting features, a virtual model cannot give the surgeon the same adherence to the operative room reality that a physical object can do. To overcome this limitation, we carried out a preliminary experience in the 3D printing of the resulting virtual model. Virtual models have to undergo a slight simplification before the printing, due to a physical limit of the 3D printing technology available (Objet 30 Pro, Objet-Stratasys). The four levels of confidence in tumor identification have to be merged into a single label that represents the maximum extent of the tumor identified by the algorithm. We included in the 3D-printed model, the pancreatic parenchyma, the tumor, and main peri-pancreatic vessels. To get an informative model, we printed the pancreatic parenchyma using a transparent photo-polymer resin, while tumor and vessels have been printed using an opaque resin (Fig. 4).

Conclusion

We presented a semiautomatic tool for the image analysis and 3D reconstruction of PDAC cases able to analyze MDCT images and to discriminate between health

pancreatic parenchyma and tumor tissue. We analyzed ten PDAC cases comparing the tumor segmentation resulting from our tool to the same segmentation manually corrected by an expert radiologist. In seven cases, the resulting model of the tumor was totally approved, as it was considered a correct and through the description of the clinical situation, while in three cases, the radiologist applied slight modifications to tumor labels.

Preliminary results show how the tool can be successfully applied to guide and support the surgeon during the evaluation of the clinical case, providing a description of the anatomy more detailed and comprehensive than the one provided by an MDCT scan. The tool showed its best performance on high-quality images, and thus, a defined acquisition protocol should be adopted. The resulting virtual model is also suitable for 3D printing, with slight simplifications, supplying to the surgeon a physical object able to provide all the anatomical information in a more direct and clear way.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Research involving human participants and/or animals This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent For this type of study formal consent is not required.

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