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Review Article

Combining Endoscopic and Radiologic Imaging: The Fusion Perspective

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Abstract

Recently new technologies has been allowing physicians to overcome the effort of combining mentally different medical information from different sources. Thanks to the latest result of computational anatomy, nowadays multimodality fusion imaging (MMFI) platforms offer the possibility to integrate ultrafast or real-time modalities - such as ultrasound or fluoroscopy - with previous cross-sectional image sets, coming from magnetic resonance imaging (MRI), computed tomography (CT) or positron emission tomography (PET). Also, endoscopy has been exploring MMFI in diagnostic and operative procedure where the only vision of the inner gastrointestinal wall could be a limiting factor. Thanks to cone-beam computed tomography, image-based navigation has been exploited successfully for easier cannulation of the major papilla in endoscopic retrograde cholangiography or for a more effective biliary drainage in an oncological setting. Fusion with 3D-CT multiplanar reconstruction improved the diagnostic capability of cholangioscopy in pre-operative assessment of cholangiocarcinoma. The placing of an electromagnetic probe in the working channel of the scope made feasible tracking its position within a cross-sectional scan and adding width and detail to the restrict endoscopic ultrasound images. It allows a better navigation in interventional EUS, such as in fine needle aspiration sampling or in drainage of pancreatic fluid collection. These first and preliminary experiences of MMFI in endoscopy are promising and need implementation.

Keywords: *Fusion Imaging; Cone-beam Computed Tomography (CBCT); Endoscopic Ultrasound; Cholangiography; Navigation; Electromagnetic Tracking*

Core tip: The concept of endoscopic navigation is revolutionizing conventional endoscopic intervention, providing operator with more precise and efficient means of diagnosis and treatment. First this review investigates various technical aspects of the pathway the lead from image acquisition to registration and fusion, where computational anatomy, cone-beam computed tomography and electromagnetic tracking are essential tools for this task. In the second part we review some preliminary and clinical experiences of fusion imaging in endoscopy and specifically in endoscopic retrograde cholangiography, peroral cholangioscopy, gastroscopy, fine needle aspiration (FNA) of abdominal and mediastinal lesions, in drainage of pancreatic fluid collections.

Introduction

Until recently, physicians used to acquire information from different modalities and in different times before planning and performing an intervention: they had to exploit their mental faculty of co-registration to combine images, data and pathological findings, by giving them an adequate spatial coherence. Indeed, each source alone provides slightly inaccurate and limited visual information that are located in a narrow field out of whole general contest. With the term "multimodality fusion imaging" (MMFI or simply "fusion imaging") we refer to the simultaneous visualization of spatially consistent and juxtaposed medical images: it includes instruments that allow personalized and tailored mini-invasive procedures and challenging interventions, thanks to a wider knowledge of anatomy, in a monitored space where it is possible to control instruments' movements and surgical actions.

MMFI rely on the precise co-registration of different image sets: it can be simultaneous - in case of integrated scanner - or sequential/retrospective, when images previously acquired are fused later. Moreover, by means of dedicated fusion platforms, real-time or ultrafast imaging modalities, such as ultrasound (US), can be combined and integrated with previous cross-sectional image sets, coming from magnetic resonance imaging (MRI), computed tomography (CT) or positron emission tomography (PET). Joining in a virtual navigation the value of a real-time, radiation free, intra-procedural monitoring with the undeniable advantages provided by a panoramic cross-sectional imaging modality results in a better awareness of the target lesion and its surroundings [1].

Digestive endoscopy itself is a real-time imaging acquisition modality. However, just for its diagnostic and operative capability limited to the "inner wall", it could result paradoxically blind and unaware of surrounding structures. To overcome these limitations for years endoscopists have learnt to deal with other tools - usually X-ray with or without contrast agents and endoscopic ultrasound - which enable them to know where they are in the abdomen and to guide consequent maneuvers beyond the gastrointestinal wall too. The radiological and ultrasonographic guides have hugely extended the clinical applications of digestive endoscopy to gastrointestinal diagnostic and operative procedures, to biopsy of extra-intestinal lesion or to drainage of abdominal liquid collections [2]. Another consequence of this opening has been the Endoscopic Retrograde Cholangiopancreatography (ERCP), in which an endoscopic image is only the starting point to obtain radiological information about another district, i.e. the biliopancreatic system.

Lately, multimodal fusion imaging has developed in endoscopy as well, especially with real-time ultrafast systems that integrate preoperative information and allow guidance to specific targets. Undoubtedly localizing targets prior to intervention is of paramount importance in an endoscopic navigation system and the computational anatomy comes for this purpose: that is a relatively new discipline that exploits several imaging modalities to overall describe human anatomy in a digital format and create accurate virtual models [3].

A widespread digital format to visualize medical images is volume rendering. It consists in displaying CT-scans or MRI scans no more separately and consecutively, but simultaneously in 3D. To see the internal structures, the initial gray level is replaced by an associated colour and transparency: this transparency gives the feeling to see delineated organs, which are not delineated in reality and need a long and difficult manual segmentation. To overcome this limit several 3D patient modelling software applications have been developed also specifically for the digestive area [4].

After a manual, interactive or automatic segmentation/extraction of boundaries and regions of interest (ROI) within 2D slices or 3D volumes, the subsequent phase of registration aligns target images from different modalities, so that relevant information from each modality can be perfectly compared [5]: the preprocedural datasets - usually 3D, i.e. CT or MRI - is matched spatially with intraprocedural imaging - usually 2D, i.e. fluoroscopy and ultrasound - by the alignment of landmarks, such as vascular structures and bones, or intensity. This procedure, called "2D/3D registration", is the precondition for "image fusion" that involves overlying the two datasets in a single view where navigation is possible [6,7].

Two navigation systems are commonly used for percutaneous procedures and has been recently tested in endoscopy: image-based tracking and external tracking. The first one often makes use of cone-beam CT (CBCT), a new technology that has been rapidly replacing the 2D fluoroscopy in interventional suite; thanks to a cone-shaped geometry between the source and a high-resolution 2D flat-panel detector, a single rotation of the CBCT C-arm is able to acquire a volumetric soft-tissue dataset, displayable in multiple planes, so as to provide multiplanar CT-like images [8]. When special navigation software from several providers identify a virtual trajectory between a skin entry point and a target structure, the 3D dataset from CBCT is mapped and overlapped onto the 2D fluoroscopic image, whatever the C-arm and table movements or image zoom, enabling the navigation [9].

Originally developed for head and neck percutaneous intervention, CBCT has quickly found application in vascular hepatic interventions, e.g. transjugular intrahepatic portosystemic shunt (TIPS) and hepatobiliary procedures, such as chemoembolization of small hepatic tumors, since its multiplanar images allow the operator not only to identify HCC but also to realize its complex vascular anatomy [10].

As for biliary interventions, Wallace., *et al*. [8] assessed the volume of liver being drained in patients with complex hilar obstructions: hence a virtual trajectory from the skin to the target biliary duct to drain can be mapped onto the live fluoroscopy and used to guide the access into the duct. Indeed, during percutaneous and endoscopic biliary drainage, 2D conventional cholangiography reveals certain disadvantages such as high exposure to radiation due to the need of several scans, the high amount of contrast agent with risk of cholangitis and the long time required for examination. Cone-beam CT navigation overcomes these limits providing immediate CT-like real-time 3D images. Nanashima first experienced these benefit in one case of gall bladder carcinoma invading hepatic hilum and in one case of hilar cholangiocarcinoma: the more accurate CBCT imaging allowed to define the exact site of biliary stenosis, to detect small abnormalities of the biliary tree due to the extension of the tumor and to release the metallic stents where useful to drain excluded hepatic segments. Moreover he verified less procedural time and contrast medium than in conventional percutaneous trans-hepatic cholangiography [11].

Later, CBCT was also applied to ERCP: after an endoscopic cholangiogram, scans acquired by a C-arm rotation are immediately rendered by a dedicated workstation and ERCP continues using the resultant 3D images. In their six consecutive cases Weigt., *et al*. found additional relevant information from 3D-ERCP compared with previous 2D-ERCP, in terms of better bile leakage localization and regarding a more accurate definition of malignant strictures extension, leading consequently to detect dilated secondary biliary ducts not yet drained after the conventional procedure. Even in two out of six patients the initial diagnosis on the basis of the conventional ERCP was dramatically changed by the 3D technique. However, it is unquestionable that CBCT involves an increased radiation exposure, so that its use could be not advisable extensively in ERCP, but only in complex cases where misdiagnosis is highly probable. Moreover, the provision of a breathing sensor becomes necessary to avoid possible artifacts resulting from breathing movements [12].

Virtual navigation through 3D images can make easier a preliminary phase of ERCP as well, i.e. the location of the major papilla and the cannulation of bile or pancreatic duct. Through a markerless camera tracking method - a feature detection technique to track the endoscopic camera without using any external marker – Nguyen., *et al*. demonstrated that is possible to register a 3D model of the organs surrounding major papilla beyond the duodenal wall, and to overlay them over the endoscopic image. It would enable the endoscopist to orientate better his maneuvers to cannulate bile or pancreatic duct, by making him explicitly aware of a wider and deeper field of view [13].

Over the years, a new diagnostic and therapeutic method, peroral cholangiopancreatoscopy (POC), has been developed allowing for direct visualisation and therapeutic manipulation of pancreaticobiliary ducts. Visual assessment and direct biopsy of a stricture using POC has been suggested as a higher accurate method for diagnosing biliary malignancy [14]. A valuable experience of fusion imaging in this field was referred in 13 patients by Nagakawa., *et al*. They fused 3D CT with multiplanar reconstruction (MPR) and cholangioscopic findings for preoperative assessment of patients with cholangiocarcinoma, in order to obtain information about both its vertical/horizontal spread (provided by CT) and superficial spread (provided by POC). Once 3D CT-cholangiography had been synchronized with cholangioscopy with almost perfect consistency, the operator marked on the virtual image the intraductal tumor extension limit and the point where biopsy had been performed. The surgical incision line chosen during hepatectomy on the basis of these data produced a R0 resection rate of 83.3%, slightly improving previous results cited in the literature [15].

Chinese engineers and surgeons demonstrated how virtual navigation in cholangioscopy is possible too. In an innovative proof of concept, they created a hollow 3D model of the biliary tree by 3D printing, from CT data of a patient with intra and extra-hepatic biliary dilatation. After a rigid registration process between CT data-derived 3D reconstruction images and the printed model, an electromagnetic sensor installed inside the cholangioscope tracked its real-time movements passing through the printed bile ducts, like a red arrow on the navigation screen. It remained to be determined whether this kind of effective pre-operative "virtual POC" can bring benefits in clinical settings [16].

A similar electromagnetic navigation was performed *in vivo* by gastrointestinal surgeons from Munich in a small case series of gastric tumor resections. Endoscopy alone cannot relate a gastric lesion to external topographic-anatomical landmarks, so that contrast-enhanced CT data become essential to assess its local involvement and to interpret endoluminal findings; both information - endoscopic and cross-sectional - are pivotal for surgery, in particular for gastro-esophageal junction tumors, but are usually provided separately. In that experience a magnetic field generator was attached with a backpack-like device to 24 patients with gastric cancer and registered the position of a miniaturized probe passed through the working channel of the scope. So the position of the tip of the scope was displayed like a cross in the previous acquired CT images with a very high accuracy. In fact, the TRE (target registration error) of this system was on average < 5 mm, obtained by measuring the distance between the cross icon of the probe and the lesion on CT plane, when the tip of the instrument was at the upper tumor margin. As for limitations of this study, two recurrent issues influencing this and other kind of navigation emerged: the difference between patient's position during CT acquisition and gastroscopy and the anatomical variations due to breath and gas insufflation [17].

These last studies were examples of external tracking navigation. With this term we refer to the use of devices - e.g. external position electromagnetic sensors - attached to surgical instruments permitting its correct localization in the pre-procedural cross-sectional imaging. Furthermore, the electromagnetic tracking is able to exploit the panoramic view of CT-scan to increase the field of vision of ultrasound, as foretold above. By now a lot of advanced ultrasound scanner are equipped with external sensors and modules of co-registration with CT, MRI and PET-CT, that enable to navigate with the US-probe observing a detailed and wide cross-sectional contrast-enhanced image [18]. Many authors valued this possibility especially in interventional ultrasound, such as in hepatic nodules treatment [19] or pancreatic fluid collection drainage [20]. For example, Mauri., *et al*. used an electromagnetic tracking platform to perform ablation of 295 hepatic tumors detectable by CT or MRI but undetectable by contrast enhanced ultrasound [21].

The same technology can be applied to the endoscopic ultrasound. However, due to the loss of 3D information on EUS, identifying CT-visible anatomical landmarks on electromagnetically tracked EUS planes is a critical and challenging point. Some researcher from UK proposed to align 2D EUS and 3D pre-procedure CT volumes using a rigid landmark-to-structure registration method, wherein organ surfaces and vessel or ductal centerlines are defined on CT images in the planning stage. Instead if specifying a point-to-point correspondence, the gastroenterologist would need only identify the corresponding CT-defined structure for each and for a minimum of three EUS landmark during the procedure. This kind of initialization showed a lower TRE when compared with a non-optimised more time-consuming initialization approach [22].

Starting from procedural studies about registration in this field, Obstein., *et al*. tested and demonstrated that Image Registration Gastroscopic Ultrasound (IRGUS) could be feasible and superior to conventional EUS in interpreting images and in reaching targets. After a rapid calibration phase based on two electromagnetic sensors (one attached at the tip of the linear echoendoscope, the other not attached) and a 3D CT-derived model, a skilled endoscopist performed examination in 5 patients: on the same monitor he found the US image, the reformatted CT image in the US defined plane and the 3D CT-based model where the US plane appeared. This fused imaging allowed the physician to quickly visualize anatomical structure without losing endoscopic ultrasound orientation, especially when the EUS image was hampered by calcification, artifacts or poor surface contact: the resulting time saving may potentially decrease sedation requirement, improve patient safety and shorten learning curve for EUS training operators. Also, for this technique, the minimal registration error was due to respiration, intra-lumen air insufflation and gravity, since the left-lateral decubitus position during endoscopy induced minimal distortion for structure located in the left upper quadrant, whereas aorta and retroperitoneal organs were quite stable [23].

An analogue more recent and advanced software was preliminary investigated by Gruionu., *et al*. in a bench-top model and in 19 patients requiring EUS-guided fine needle aspiration (FNA) for defining mediastinal, lymph nodal or pancreatic lesions. Using a navigation catheter with 6 degree of freedom placed in the working-channel of the echoendoscope, they used only the hybrid CT-EUS image for FNA guidance, with the possibility to accomplish manually in real-time fine adjustments of the registration through rotation and translation of the CT image using a 3D mouse. The CT-EUS fusion imaging did not add significant extra-procedural time, although the co-registration had to be realigned several times during the procedure. The precision of simultaneous CT-EUS visualization was evaluated as high in 80% of cases, suggesting that the system is accurate at depicting the target lesion, enabling at the same time the endoscopist to visualize both its EUS and contrast-enhanced-CT features [24].

Our center has recently implemented an innovative fusion system of pre-procedural CT and real-time EUS and fluoroscopy in pancreatic fluid collection (PFC) drainage. After a manual segmentation of pre-procedural CT images, the resultant region of interest (ROI) including PFC is placed on the volume rendering derived from CT-scan, in turn registered to intra-procedural fluoroscopy with two orthogonal X-ray matching anatomical landmark (vertebrae or iliac crests). Ultimately for every intraprocedural fluoroscopy, whatever the C-arm movement, a simultaneous visualization of the scope tip and of the whole PFC shape in the correct position is available, improving the choice of the puncture-site especially in complex abdominal collections. In a study in course of publication we compare the clinical outcome of this new to the conventional approach in 35 subjects: though limited by the inhomogeneity of the populations, our results suggest a better and more rapid emptying of the drained collection associated with an improvement of symptoms for patients treated with the fusion modality [25].

Conclusion

Even though the attempts to use fusion imaging in endoscopy are preliminary, scarce and based on few patients, they seem to be promising and need implementation. In the future the demonstrated feasibility of consolidated tracking techniques might allow to widen further indications for trying fusion of endoscopic and radiological images, e.g. virtual colonoscopy or enteroscopy and in the characterization of sub-epithelial lesions. Moreover, advanced navigation platforms are interesting and raising tools for guiding personalized and tailored mini-invasive interventional procedures. The availability of these new diagnostic and therapeutic information can increase the operator's confidence in his acts and leading closer to a "precision surgery".

Conflict of Interest Statement

Authors declare no conflict of interests for this article.

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