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Research Paper

Experimental analysis of the mechanical behavior of the viscoelastic porcine pancreas and preliminary case study on the human pancreas

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ABSTRACT

The aim of this article is to study the mechanical properties of the pancreas. Up to now, the mechanical properties of the pancreas are not sufficiently characterized. The possibility of intraoperative mechanical testing of pathological pancreata will allow the classification of pancreatic diseases in the future. The application of mechanical parameters instead of the intraoperative frozen section analysis shortens waiting times in the operating room. This study proves the general applicability of shear rheology for the determination of the mechanical properties of pancreas and the assessment of graft quality for transplantation. Porcine and human pancreas samples were examined *ex vivo* and a nonlinear viscoelastic behavior was observed. Pancreas was found to be more viscous than liver but both abdominal organs showed a similar flow behavior. The shear deformation dependence of healthy human pancreas was similar to porcine pancreas. An increase in the *post-mortem* time led to an increase in the complex modulus for a *post-mortem* time up to 8.5 days. Histological investigations showed that an increased amount of collagen coincides with the stiffening of the pancreatic tissue.

1. Introduction

Although pancreas transplantation has gained significant popularity during the past decade, it has the highest surgical complication rate of all routinely performed solid organ transplants (Humar et al., 2000). Reasons for this are difficulties in the surgical technique, graft rejection or an unfavorable choice of donor and recipient. Grafts are selected from living donors or as cadaveric grafts. Cadaveric pancreas allocation is not based on diabetes severity but rather depends on blood type and time on the waiting list (Venstrom et al., 2003). The transplantation of live grafts is associated with higher graft survival rates due to a lower incidence of rejection, compared with cadaveric transplants. But only a small part of all transplanted grafts are from living donors. There is currently no shortage of cadaveric pancreases if matching is ignored (Gruessner et al., 1997). With mostly cadaveric pancreas grafts used, a method of

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quantification of the quality of the graft is needed to avoid complications or failure of the transplantation. Thus, a first step will be to define the mechanical properties of healthy pancreatic tissue *ex vivo*. Once standard values are established, another aim of this study is to find a potential mechanical parameter to evaluate the quality of a graft or the type and progress of a disease. To date, no characterization of the donated graft is conducted to the authors' knowledge. Therefore, the transplant surgeon has no knowledge of the actual state and characteristics of the organ. Up to now, the characterization of potentially malignant pancreatic tissue is only possible with the help of biopsy and histology or with medical imaging such as sonography, computed tomography or magnetic resonance imaging (Bipat et al., 2005; Liu and Bilston 2000; Ophir et al., 2002). Tissue elasticity imaging methods based on ultrasonics currently fall into two main groups. The first group consists of methods where a quasi-static compression is applied to the tissue and the resulting components of the strain tensor are estimated. Group 2 contains methods where a low frequency vibration is applied to the tissue and the resulting tissue behavior is inspected by ultrasonics or audible acoustic means.

Although elastography is a good method to distinguish between healthy soft tissue and stiffer, potentially malignant areas, it does not reliably differentiate between benign and malignant pancreatic lesions (Giovannini et al., 2009). Another major limitation of EUS elastography is the endosonographer's inability to control tissue compression. Strong pressure on the tissue can result in a misdiagnosis. Another difficulty is missing soft tissue surrounding the target zone and the presence of the aorta or the spine which leads to artifacts caused by these rigid tissues (Arcidiacono, 2012). A more general problem concerning all diagnostic procedures based on stiffness measurements is the fact that the stiffness of benign and malignant lesions may overlap. For example, some cancers may be soft, resulting in a false negative elastogram. Similarly, some benign lesions may appear stiff including hyalinized fibroadenomas, fat necrosis and fibrosis (Evans et al., 2012). Thus, a characteristic indicator must be found, which shows a distinct relationship between disease and magnitude of the measured mechanical parameter.

To date, most clinical studies dealing with the diagnosis of pancreatic diseases apply medical imaging which is conducted *in vivo*. The *in vivo* shear stiffness of pancreas was for example investigated with the MR elastography technique (Yin et al., 2008) and found to be 2.0 ± 0.4kPa which is similar to that of hepatic tissue (Rouviere et al., 2006). Similar investigations were conducted (Shi et al., 2014) with a resulting mean shear stiffness of 1.2 kPa at 40 Hz and 2.1 kPa at 60 Hz, respectively.

Due to its location in the back of the abdomen, diagnosing pancreatic lesions generally require a multimodality approach of methods including qualitative approaches such as computed tomography, magnetic resonance imaging and endoscopic ultrasound (EUS) (Wallace and Hawes, 2001; Yin et al., 2009; Chaudhary and Bano, 2011) and the quantitative method fine needle aspiration (Iglesias–Garcia et al., 2010). The physician has to keep in mind that imaging methods only result in qualitative images of stiffness (Greenleaf et al., 2003). However, with all their advantages and limitations a combination of these conventional methods gives the physician the best prognosis about the state of health of the pancreas. The future efficacy of the elasticity measurement/imaging methods in medicine depends on image contrast and resolution in addition to acquisition speed and cost (Greenleaf et al., 2003). Even though currently used *in vivo* methods are considered save (Voss et al., 2000), the application of fine needle aspiration can infrequently lead to acute pancreatitis or aspiration pneumonia (O'Toole et al., 2001). The imaging technique computed tomography has the disadvantage of radiation while magnetic resonance imaging can only be conducted on patients without metal implants. Very infrequent complications of endoscopic ultrasound are tearing of the linings of oesophagus, stomach or duodenum or bleeding. For more information about medical imaging of the pancreas the authors refer to (Yin et al., 2008; Janssen et al., 2007; Schrader et al., 2012).

In addition to medical imaging methods only two other papers (Nicolle et al., 2013; Vito et al., 1981) have appeared concerning the mechanical properties of pancreas. In 1981, Vito et al. Vito et al., (1981) conducted tensile tests on normal and pseudocystic pancreatic tissue and did not observe significant differences in the material behavior. Pancreatic tissue was characterized as viscoelastic. In 2013, Nicolle et al. Nicolle et al., (2013) conducted shear rheological experiments to characterize the frequency dependence of porcine pancreas. Pancreas was found to be more viscous than other abdominal organs such as kidney, liver and spleen. A low frequency-dependent dynamic modulus ranging from 120 to 180 Pa between 0.1 and 0.8 Hz was observed.

There is limited knowledge about the mechanical properties of pancreas and how they change with the onset of necrosis and fibrosis in chronic pancreatitis (Janssen et al., 2007). For diagnostics, it is assumed that the pancreatic shear stiffness increases with the degree of fibrosis similar to that in liver tissue (Georges et al., 2007; Ziol et al., 2005). The question is now whether pancreatic diseases, which are up to now securely detectable only through biopsy can also be identified with the help of intraoperative mechanical methods such as indentation, palpation or the application of rotational devices. In the future, the authors will try to prove the general applicability of such methods for the diagnosis of pancreatic diseases instead of taking samples and risking the formation of fistulas or pancreatitis. The development of a diagnostic tool to measure mechanical parameters intraoperatively can be the next step forward. The *in vivo* mechanical diagnostic tool will be applicable for open surgery only. Issues such as safety, sterilizability, space limitation and a short data acquisition cycle time will have to be addressed concerning this matter.

However, the aim of this study is to describe the mechanical properties of the pancreas. Therefore, the article tries to assess different aspects. The use of both porcine and human pancreatic tissue allows a comparison of the two tissue types. Furthermore, pancreas is compared with the viscoelastic properties of another abdominal organ – the liver. The influence of the *post-mortem* time (pmt) on the mechanical behavior is investigated and lastly but most importantly the influence of the state of health on the mechanics of the pancreas is studied.