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EVALUATING OPTICAL COHERENCE ELASTOGRAPHY FOR DETECTION OF GASTRIC CANCER AND HIGH-GRADE DYSPLASIA BY MEASURING MECHANICAL ALTERATION IN EX-VIVO HUMAN GASTRIC SPECIMENS.

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INTRODUCTION

Gastric cancer has a high morbidity and mortality with a 5-year survival rate below 35% due to a lack of effective detection and localization methods.[1] This is particularly the case with high-grade dysplasia and submucosal tumors such as linitis plastica, which often evade detection by endoscopy. We describe the use of Optical Coherence Elastography (OCE) for the detection, localization, and staging of high-grade dysplasia (HGD) and gastric cancer (GC). OCE is an emerging method for characterizing the mechanical properties of tissue that utilizes optical coherence tomography for depth-resolved structural imaging; it leverages information of applied force to generate spatially resolved maps of tissue stiffness that are altered in the architectural changes of neoplasia.[2] It is uniquely suited for detecting HGD and sub-mucosal gastric cancer, given the depth-resolved and high-resolution image data. Such a technology could be implemented endoscopically for point-of-care detection of HGD and early cancer, but first, the sensitivity to disease must be evaluated through *ex vivo* studies.

AIM

Evaluate the utility of optical coherence elastography for gastric cancer and high-grade dysplasia detection.

METHOD

We performed ex vivo imaging on gastric cancer (n= 3), HGD (n= 2) specimens, and matched normal tissue controls (n=5) from five patients undergoing surgical resection or endoscopic biopsy for cancer or HGD. OCE data was collected using an "optical palpation" approach by measuring the compression of overlying tissue phantoms and iteratively increasing the applied force.[3] Stiffness was calculated for normal and cancer regions using an automated algorithm to evaluate displacement as a function of applied force.[4]

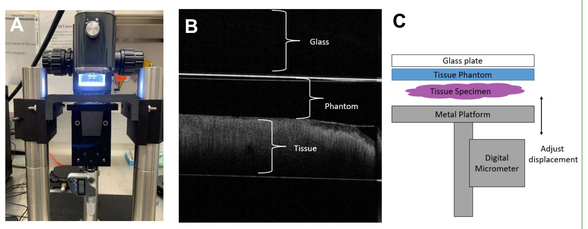

Figure 1: Experimental setup used for studies to evaluate OCE for gastric cancer detection. (A) Photograph of the OCE system with optical palpation approach. (B) An example image collected from the system shows different interfaces. (C) A diagram of how force is increased by adjusting the metal platform height.

RESULTS

Our results show that OCE imaging can visualize structural changes in neoplastic tissue and later-stage cancer. Figure 2 shows qualitative OCT images of normal gastric cardia and signet cell cancer, where clear structural changes are visible between the two. Quantification of image data suggests that tissue stiffness increases with the onset of disease, particularly with HGD, as well as adenocarcinoma, as shown in Figure 3. In all specimens, the tissue stiffness is measured to be higher in abnormal tissues than normal tissue controls. Figure 4 illustrates how OCE can be used to provide a spatial mapping of stiffness – this surgical tissue specimen exhibited the boundary between normal and diseased tissue, for which the stiffness is clearly increased in the diseased region. Ultimately, these promising results demonstrate that early tissue stiffness changes could be leveraged for diagnostic purposes.

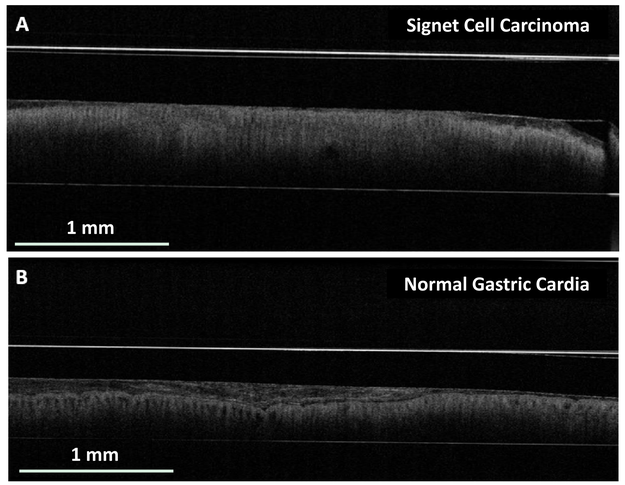

Figure 2: Optical coherence elastography images of ex vivo samples of (A) signet cell carcinoma and (B) normal gastric cardia, showing alterations in qualitative imaging features.

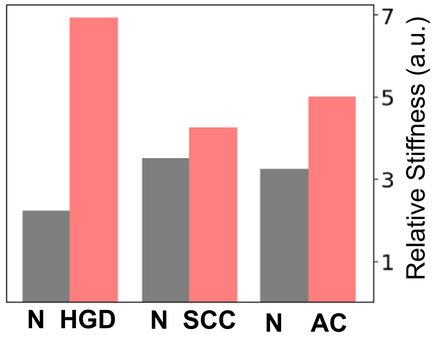

Figure 3: (A) Bar chart showing tissue stiffness for three match patient samples of different types of disease. All three patients showed increased tissue stiffness for diseased tissues as measured by OCE. N= normal gastric cardia, HGD = high grade dysplasia; SCC = signet cell carcinoma; AC = adenocarcinoma.

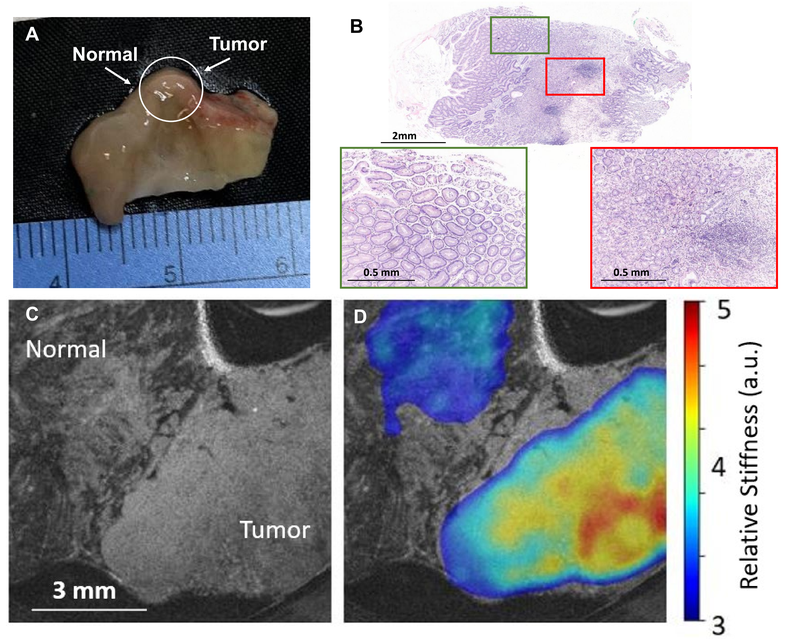

Figure 4: (A) Photograph of resected gastric cancer specimen with transition zone between normal and adenocarcinoma tumor. (B) Histology image of the surgical sample showing the transition zone between disease and normal tissue. (C) en face optical coherence elastography image of the specimen in (A), with (D) heat map showing relative stiffness, indicating increased stiffness of diseased tissues.

CONCLUSIONS

In summary, the data from this study suggests that OCE is a promising imaging modality for detecting mechanical alterations in tissue due to HGD or GC. Its ability to detect HGD may be particularly useful for early detection of submucosal cancer, as this technology can be implemented in endoscopic imaging for point-of-care diagnosis and screening. Moreover, OCE's ability to detect and localize HGD and GC may facilitate their effective endoscopic removal using endoscopic submucosal dissection.

While promising, several important limitations are acknowledged, namely the limited sample size and the fact that the study was conducted on *ex vivo* tissue specimens, which do not fully recapitulate *in vivo* characteristics.

The next steps for this work include increasing the dataset to assess patient-to-patient variability, as well as validation of the overall premise on *in vivo* tissue specimens, potentially by leveraging animal models of gastric cancer. In addition, the development of *in vivo* capable technology remains an active area of research to enable the downstream clinical translation of this technology to address the clinical need for early detection of gastric cancer.

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