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Contrast-Enhanced Endoscopic Ultrasound for Identification of Sentinel Lymph Nodes in Esophageal Cancer

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- Esophageal Carcinoma
 - Estimated 18,400 new cases in the US in 2020
 - 5 year survival between 19% – 22%
- Tumor Staging for Esophageal Carcinoma
 - Sentinel Lymph Node identification and staging
 - Endoscopic Ultrasound Guided Biopsy – 38% - 51% accuracy
 - Radionuclide, Blue Dye, and CT – 85% accuracy
 - Prognostic significance

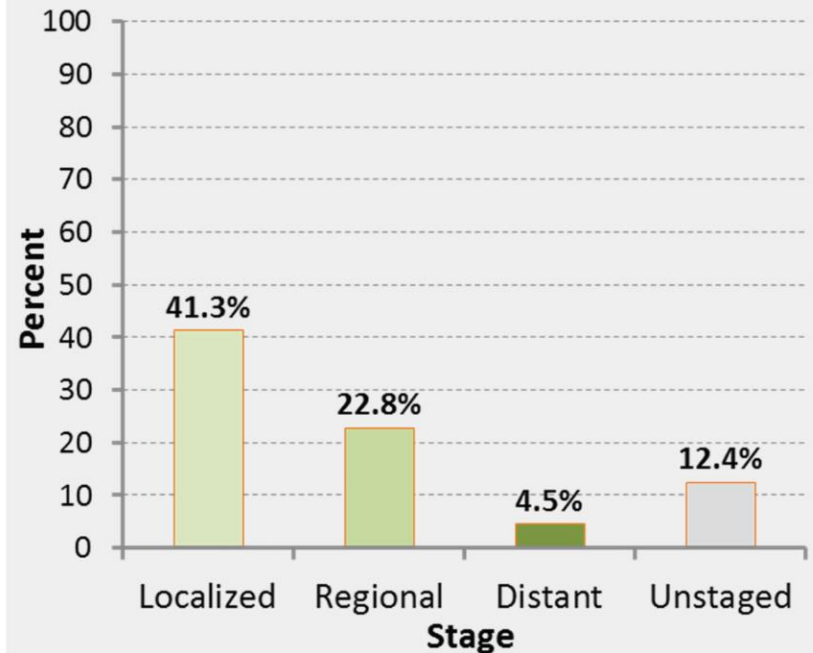
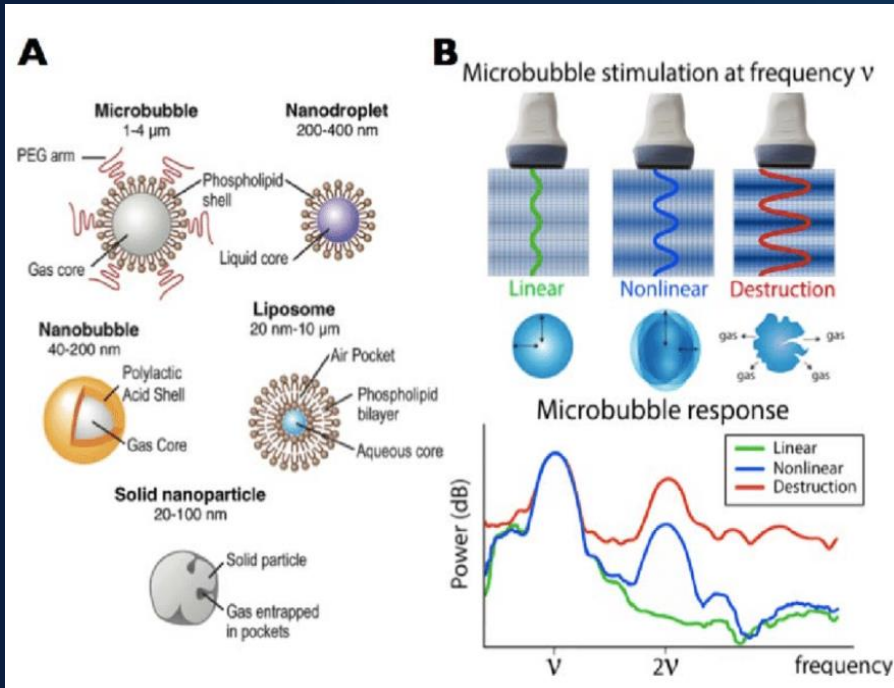


Figure 1. 5 Year survival rates of esophageal cancer by staging [SEER 2010].



- Contrast Enhanced Endoscopic Lymphsonography (CEUS)
 - Enhanced imaging of lymph nodes using Ultrasound Contrast Agents
 - “Contrast-Enhanced Ultrasound Imaging of Sentinel Lymph Nodes After Peritumoral Administration of Sonazoid in a Melanoma Tumor Animal Model”
 - Goldberg et al
 - 82% accuracy in detecting Sentinel Lymph Nodes (SLN)

Objectives & Hypothesis

- Research Question
 - How will Contrast Enhanced Lymphsonography (CEUS) compare to Endoscopic Ultrasound (EUS) in the identification of Sentinel Lymph Nodes and overall tumor staging in adult patients with esophageal carcinoma?
- Hypothesis
 - The use of CEUS in lymph node biopsy will increase the percentage of malignancy positive SLNs biopsied as compared to EUS and provide more accurate tumor staging.

Approach & Results

- Study design
 - Unblinded Pilot Study
- Population / study sample
 - 40 patients at TJUH recently diagnosed with esophageal carcinoma
- Intervention
 - Contrast Enhanced Lymphsonography
- Data source and collection
 - Comparison of patient's contrast enhanced exam with their own unenhanced exam
 - All patients will undergo non-contrast EUS and suspicious nodes will be identified and biopsied (standard of care)
 - Peritumor injection of ultrasound contrast agent, Sonazoid, will be administered and suspicious nodes by CEUS will be biopsied
 - All biopsied specimens will be assessed for presence of cancer spread by qualified pathologist

Approach & Results

- Analysis
 - Calculation of metastasis identification, accuracy of SLN identification, sensitivity, specificity, PPV, and NPV of CEUS and EUS sampled lymph nodes
 - Pathology as reference standard
- Findings

	Nodes Enhanced on CEUS	Nodes Unenhanced on CEUS	
High risk by EUS	Nodes: 6 Path Results: 2 benign 2 indeterminate/unaccessible 2 malignant	Nodes:15 Path Results: 1 benign 12 unaccessible 2 malignant	21
Low risk by EUS	Nodes: 13 Path Results: 3 benign 10 malignant	Nodes: 21 Path Results: 20 untested 1 malignant	34
	19	36	55

Conclusions

- EUS-guided FNA biopsy - metastasis positive rate of 40% (10/20)
- CEUS-guided biopsy - metastasis positive rate of 63% (12/19)
- 4 participants (29%) had nodal status upgrade with the addition of CE-EUS findings
 - altering their clinical management and future course of therapy

CEUS guided FNA

- Accuracy – 61.9%
- Sensitivity – 80%
- Specificity – 16.7%
- PPV – 70.6%
- NPV – 25%

EUS guided FNA

- Accuracy – 33.3%
- Sensitivity – 26.7%
- Specificity – 50%
- PPV – 57.1%
- NPV – 21.4%

CE-EUS identification and FNA of SLN may increase cytologic yield by ruling out nodes not associated with the tumor drainage pattern and identifying SLNs with metastatic deposits not seen by EUS. These findings highlight the current shortcomings of EUS nodal staging in esophageal cancer and the important clinical improvements that can be achieved even by modestly improving SLN identification.

Future Directions

- Larger trial to improve statistical significance
 - Increase length of the study to follow clinical outcomes
- Comparison of different contrast agents
- Effectiveness of Ultrasound Contrast Agent in different cancers

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