

ADVANCES IN ENDOSCOPY

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Endoscopic Ultrasound–Guided Fiducial Placement for Gastrointestinal Malignancies



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G&H What are fiducial markers, and why are they used?

JH Fiducials are metallic or liquid radiopaque markers that are inserted near or into a target lesion and act as internal landmarks that enable real-time lesion tracking. Fiducial markers come in various shapes and sizes and can be made of gold, carbon, platinum, or polymer. Gold markers are currently the most commonly used type. Fiducial markers serve as reference points for image-guided radiotherapy. The visualization of fiducials allows for high doses of radiation to be delivered with increased accuracy by quantifying respiratory motion and tumor extent, thus limiting exposure of the surrounding healthy tissue.

G&H What is the role of fiducial markers in the setting of gastroenterology?

MB The role of radiotherapy in the neoadjuvant, adjuvant, or palliative setting of gastrointestinal (GI) malignancies is continuously evolving. In order to safely deliver a higher dose of radiation to GI tumors, an

accurate evaluation of tumor size and location during respiration is necessary. In the absence of diagnostic, quality on-board computed tomography (CT)-on-rails or magnetic resonance imaging, accurate delivery of image-guided radiotherapy relies on fiducial markers. Initially, fiducial markers were placed surgically or percutaneously under CT or ultrasound guidance. However, surgery is invasive, and the percutaneous approach is associated with a high risk for organ and vascular damage. Endoscopic ultrasound (EUS) has the capability to provide high-resolution visualization of the deep structures within the abdomen and mediastinum, which overcomes some of the limitations of percutaneous insertion. Furthermore, EUS offers a less-invasive approach than surgery. In the past decade, EUS has evolved as a safe and minimally invasive approach for the placement of fiducial markers. The first EUS-guided fiducial placement in patients with pancreatic cancer was reported in 2006, and the procedure proved to be safe and technically feasible. It has become the preferred approach for fiducial marker placement for lesions within or adjacent to the GI lumen. EUS-guided fiducial placement has been reported for nearly all GI

malignancies, including pancreatic, hepatic, esophageal, gastric, and colorectal tumors.

G&H How does the type and size of the needle affect EUS-guided fiducial placement?

MB Various types of fiducial markers and different delivery systems have been developed thus far. Generally, the size and shape of the fiducial dictates the type of needle that should be used. Fiducials can be delivered

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through 19-, 22-, or 25-gauge needles or multifiducial delivery systems. Initially, because of the broad diameter of traditional fiducials, EUS-guided fiducial placement was performed using 19-gauge fine-needle aspiration (FNA) needles. Although the application of this needle proved to be feasible and safe in various target organs, its stiffness may compromise the placement of fiducial markers in the targeted lesion. Thus, a 22-gauge needle can be used in challenging anatomic locations or post-surgical anatomy due to its greater flexibility.

G&H Have any studies compared the use of preloaded devices with that of traditional hand-loaded devices for EUS-guided fiducial placement?

MB Data are limited to recommend the optimal type of fiducial to be placed under EUS guidance. Multifiducial delivery systems are commercially available for use. One type of preloaded needle is available in 2 sizes (19- or 22-gauge) and is loaded with 2 fiducials. Another 22-gauge preloaded needle has been developed and is loaded with 4 fiducials. These multifiducial delivery systems were developed to improve the efficacy and efficiency of EUS-guided fiducial placement. However, there is no evidence that preloaded devices have better

results than traditional hand-loaded devices, although they appear to be time- and labor-saving given the reduced need for setup prior to the procedure.

G&H Where should fiducials be placed in order to mark GI malignancies?

MB Pancreatic cancer has been the most extensively studied malignancy regarding the role of EUS-guided fiducial placement. For pancreatic tumors, the EUS-guided placement of at least 3 fiducial markers is recommended. Fiducials are attempted to be placed into the tumor and/or periphery, preferably in different EUS planes, and within locations that would define tumor border and planes. EUS-guided fiducial placement can be performed during the time of a scheduled EUS-guided FNA. Some authors suggest that performing both EUS-FNA and fiducial placement during the same procedure may cause trauma and extend anesthesia time, possibly leading to a higher risk of procedure-related adverse events. However, given the controversies in the management of pancreatic cancer, fiducials are not typically placed upfront at the time of EUS-FNA and staging. For esophageal tumors, fiducial markers are typically placed into the submucosa just proximal or distal to the tumor. For rectal tumors, fiducials are inserted at the superior and inferior extents as well as sometimes in the center of the tumor. There are no specific guidelines established for the number of fiducial markers placed per patient.

G&H How do traditional fiducials compare with coiled fiducials?

MB A retrospective study comparing traditional fiducials to flexible coiled fiducials in patients with advanced pancreatic cancer demonstrated comparable technical success with no difference in migration or complication between the 2 types of fiducials. However, the visibility of traditional fiducials was significantly better than that of the coiled fiducials on CT scans and during subsequent image-guided radiotherapy, possibly due to their larger diameter.

G&H What other aspects should be considered when placing fiducial markers for GI malignancies?

MB Various techniques for fiducial marker loading and deployment have been described. There are no controlled studies comparing how these different techniques perform, and it is difficult to establish comparisons given the differences in target lesion locations and characteristics.

JH The decision to incorporate fiducial markers in the treatment plan of a patient depends on the multidisciplinary collaboration between gastroenterologists and radiation, medical, and surgical oncologists. Fiducial tracking is typically preferred when available, and there is evidence that it improves the accuracy of daily target delineation during image-guided radiotherapy. Another important aspect to consider is the fact that endoscopic fiducial placement also offers a chance to evaluate the stomach and duodenum for any preexisting injury or ulcers or involvement by the tumor (eg, pancreas), which may inform radiation oncologists about what dose can be safely given.

G&H Could you explain the findings of your systematic review on EUS-guided fiducial placement?

MB Further research was needed concerning safety and technical aspects of this procedure due to the increasing demand for EUS-guided fiducial placement. My colleagues and I conducted the first meta-analysis evaluating the technical success and safety of EUS fiducial placement for image-guided radiotherapy in GI malignancies. More than 1000 patients with confirmed GI cancers who underwent EUS for fiducial placement were included. According to our meta-analysis, EUS-guided fiducial placement is technically feasible with an overall success rate of 98%, suggesting that this procedure can be performed routinely with high success

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rates. Moreover, although spontaneous migration can occur, the overall rate of fiducial migration, according to our results, was only 3%, and no migration-related complications were reported. Our meta-analysis yielded an adverse event rate of 4%, indicating that EUS-guided fiducial placement is also a safe procedure.

G&H What were the limitations of your systematic review and meta-analysis?

MB Our systematic review and meta-analysis had a few limitations that should be acknowledged. One is the significant heterogeneity between the studies, which appeared to be caused by a very large sample size of one of the studies included in the analysis. Different methodologies and techniques used for the placement of fiducials and the varying types of cancer that were targeted may have contributed to heterogeneity within our study. Also, all studies included in the meta-analysis were published in English; therefore, studies published in other languages that could have contributed significant data may have been missed. Publication bias was present for the assessment of success rate, suggesting that negative-outcome studies may have not been published.

G&H What adverse events are associated with EUS-guided fiducial placement?

MB EUS-guided fiducial placement is a safe procedure. No major life-threatening adverse events have been reported thus far, but care must be employed when performing this procedure in order to avoid intervening vessels and to ensure placement into the proper target tissue. Reported adverse events included mild acute pancreatitis, minor bleeding, fever, abdominal pain, rectal pain, and elevated liver enzymes. Based on a report of procedure-related cholangitis in fiducial markers placed for pancreatic cancer, prophylactic antibiotics were recommended, although strong evidence for this indication is not available. At our institution, patients receive prophylactic antibiotics during or before the procedure.

G&H What is the long-term effectiveness of fiducial placement for GI malignancies?

JH There is no evidence of fiducial-related long-term complications. Future studies are expected to shed further light on the clinical and survival benefits of fiducial markers in patients with GI malignancies.

G&H What are the barriers to the widespread use of EUS-guided fiducials?

JH Not many centers have had experience with fiducial placement. Providers' lack of understanding of the value of using a fiducial is the main barrier that limits the widespread use of fiducial markers.

G&H What are the priorities of research in this field?

MB At our institution, we have a dedicated team working on research projects involving different clinical and technical aspects of fiducial markers. Studies are underway to determine the optimal type of fiducials to be placed under EUS guidance. Our team of researchers (Drs Sam Beddar, Jordan Slagowski, Irina Cazacu, and Ben Singh) is investigating the visibility and level of artifact associated with the various types of fiducials.

JH We are also assessing new liquid fiducial markers. Our group (Drs Cullen Taniguchi, Eugene Koay, and Shalini Moningi) is evaluating the local tumor control, radiation toxicity, and overall survival for patients who received radiotherapy with fiducial markers vs radiotherapy without fiducials, as currently there are no randomized, controlled trials comparing these issues between the 2 patient populations. All of this work is expected to clarify the use of EUS-guided fiducial placement in GI malignancies.

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Suggested Reading

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