Endoscopic ultrasound-guided fiducial marker placement for image-guided radiation therapy without fluoroscopy: safety and technical feasibility

Authors Gautamy Chitiki Dhadham[1], Sarah Hoffe[2], Cynthia L. Harris[1], Jason B. Klapman[1]

Institutions
[1] Gastrointestinal Tumor Program, Division of Endoscopic Oncology, Moffitt Cancer Center & Research Institute, Tampa, Florida, United States
[2] Department of Radiation Oncology, Moffitt Cancer Center & Research Institute, Tampa, Florida, United States

Bibliography
DOI http://dx.doi.org/10.1055/s-0042-100720
Published online: 3.3.2016
Endoscopy International Open 2016; 04: E378–E382

E-ISSN 2196-9736

Corresponding Author
Jason Klapman, MD, FASGE
Director of Endoscopy
Gastrointestinal Tumor Program
Moffitt Cancer Center
Associate Professor of Medicine
Department of Oncologic Sciences
University of South Florida
12902 Magnolia Drive
Tampa, FL 33612
Fax: +1-813-745-7229
jason.klapman@moffitt.org

Background and study aims: Endoscopic ultrasound (EUS)-guided fiducial marker placement for image-guided radiation treatment (IGRT) is becoming more widespread. Most case series report the procedure performed using fluoroscopy for spatial geometry although the benefits of this are unclear. The aim of our study is to report the technical feasibility, safety, and migration rate of fiducial marker placement in a large cohort of patients with gastrointestinal malignancies who underwent EUS-guided fiducial marker placement for IGRT without fluoroscopy.

Patients and methods: A retrospective chart review was performed on all patients referred for EUS-guided fiducial marker placement from 08/1/07 to 7/31/14 at Moffitt Cancer Center.

Results: During the study period, 514 patients underwent placement of 1093 gold fiducial markers under EUS-guidance. Two hundred and forty patients with esophageal/gastro-esophageal junction cancer had 405 fiducials placed. In 188 patients with pancreatic ancer, 510 fiducials were placed. In 54 patients with rectal cancer, 103 fiducials were placed and 32 patients had 75 fiducials placed into other gastrointestinal tract lesions. Minor bleeding, which resolved spontaneously, occurred in two patients. Technical difficulty in placing fiducials was noted in 18 patients. Intraprocedural fiducial migration was noted in two patients and only 2/1093 fiducials (.002%) in two esophageal patients migrated as noted on simulation computed tomography scan.

Conclusions: EUS-guided fiducial marker placement without fluoroscopy is technically feasible and safe. There were minimal intraprocedure/post-procedure complications. Imaging at the time of simulation also revealed the migration rate to be extremely low. These results may allow for more widespread adoption of EUS-guided fiducial marker placement.

Introduction

Image-guided radiation therapy (IGRT) for the treatment of gastrointestinal cancers is enhanced by fiducial markers placed for tumor localization, which allows for precise targeting of the tumor, taking into account the respiratory motion of the target lesion during radiation therapy [1]. This technique minimizes toxicity to adjacent organs. Until recently, fiducial marker placement was performed either intraoperatively, percutaneously or via the computed tomography (CT)-guided approach [2]. With the evolution of interventional EUS, EUS-guided placement of fiducial markers for esophageal, pancreatic, and rectal malignancies is increasing in popularity [1,3]. Most of the current published literature on this technique describes performing the procedure with the aid of fluoroscopy to improve the spatial geometry of fiducials placed but the benefits of this are unclear. At our center we routinely place EUS-guided fiducials without the aid of fluoroscopy. There are also limited published data on the technical feasibility, safety, and migration rate of EUS-guided fiducial placement. Studies have addressed the placement of fiducials using different size needles and in different abdominal and mediastinal locations in a limited number of patients [3–6]. Only one recent study has reported on the technical feasibility and stability of fiducial markers that were placed under EUS guidance alone for pancreatic and hepatic malignancies, but in a limited number of patients [3]. Assessment of the feasibility and complications using this technique is limited in the literature. With increasing demand for this procedure, further knowledge is needed on different techniques for performing the procedure and their associated adverse event and migration rates. We thus set out to review and report our center's experience with EUS-guided fiducial marker placement without the aid of fluoroscopy.

Patients and methods

Patients

We retrospectively reviewed an institutional review board (IRB)-approved database (University of South Florida IRB #Pro00019208) of all patients who had undergone EUS-guided fiducials for gastrointestinal malignancies. Patient characteristics, including, age, gender, date of fiducial placement, number and size of fiducials placed, size of needle used, technical feasibility in placing fiducials, type of gastrointestinal malignancy, complications, and stability of EUS-guided fiducial placement for IGRT in the last 7 years (August 1, 2007 – July 31, 2014) were obtained. Baseline patient characteristics are summarized in **Table 1**.

EUS-guided fiducial placement

All patients underwent EUS with a linear-array echoendoscope (GF-UC140P-AL5; Olympus America, Center Valley, PA) under propofol-administered monitored anesthesia. For the majority of patients, a 19-gauge or 22-gauge EUS-FNA needle (Cook Endoscopy, Winston Salem, NC) was used for fiducial placement. After withdrawing the stylet, 7 to 8 mm from the needle, a gold cylindrical fiducial marker measuring 0.75 × 10 mm or 0.35 × 10 mm (Visicoil, RadioMed, Inc, Tingsboro, MA) was back loaded into the 19-gauge or 22-gauge needle tip, respectively, by using sterile forceps and then sealed into place with sterile bone wax. The needle was then advanced via the operating channel of the echoendoscope without losing the fiducial. Once a safe insertion window away from blood vessels was identified on doppler echoendosonography, the needle was then inserted into the target area under EUS guidance. Upon needle insertion into or adjacent to the target lesion, the fiducial was deployed by simultaneously retracting the needle while advancing the stylet. The needle was then withdrawn from the echoendoscope and reloaded with a new fiducial, and the technique repeated until the desired number of markers had been placed. All fiducials were placed under EUS guidance alone; fluoroscopy was not used. All endoscopy procedure reports, post-procedure orders, 24-hour post-procedure telephone notes, and all electronic medical record entries occurring in the 4 weeks after fiducial placement were reviewed to determine if any early (defined as within 72 hours) or late (72 hours to 30 days post-procedure) complications related to fiducial placement occurred.

Timing of fiducial marker placement

For patients with esophageal and rectal cancers, fiducial markers were placed at the time of initial EUS staging. For pancreatic cancer, all patients at our institution were treated initially with systemic chemotherapy. We did not place the fiducial markers upfront at the time of initial staging and fine-needle aspiration because not all of those patients were candidates for local therapy after chemotherapy. If, after systemic chemotherapy, there was no evidence of progression, the patients were considered for radiation. We performed endoscopic ultrasound evaluation at that time point to reassess the response to therapy and to place fiducial markers. We believe that this strategy prevents unnecessary fiducial marker placement in patients who have evidence of disease progression and will not receive local radiation therapy.

Table 1 Patient characteristics.

Characteristic	No. (value)
No. of patients	514
No. of fiducials	1093
Age (Y)	
Median	67
Range	31 – 91
Sex	
Male	358 (70 %)
Female	156 (30 %)
Primary tumor location	
Esophagus	207 (40 %)
GE junction	33 (7 %)
Pancreas	188 (37 %)
Rectal	54 (11 %)
Others	32 (5 %)

No., number; Y, year; GE, gastroesophageal

Results

A total of 514 patients underwent placement of 1093 fiducials under EUS guidance during the study period. Fiducial placement was unsuccessful in only a single patient with pancreatic cancer because intervening blood vessels precluded safe advancement of the fiducials into the mass. In subgroup analysis there was no statistical difference between the 19-gauge and 22-gauge needle placement of fiducials with respect to adverse events or fiducial migration. The location, number of fiducials placed, technical difficulty, and rates of migration and adverse events are summarized in **Table 2**.

Esophageal cancer

Two hundred and seven patients with esophageal cancer had a total of 348 fiducials inserted. A 19-gauge needle back loaded with a 0.75 × 10 mm Visicoil gold fiducial marker was used in the majority of patients (n = 188 [90.8 %]), while a 22-gauge needle back loaded with a 0.35 × 10 mm fiducial was used in 11 patients (5.3 %) . In a small number of patients (5), a 25-gauge needle back loaded with a 0.35 × 10 mm fiducial was used. Both a 19 – and 22-gauge needle were used in one (0.5 %) and the gauge was unknown in two (1 %). Fiducials could be inserted proximal and distal to the tumor in 112 patients, whereas only proximal fiducials could be placed in 82 patients (due to luminal obstruction) and only distal fiducial placement was possible in one patient. In a small subset of patients (12), the fiducial was placed into the bulk of the tumor due to inability to place a marker at the proximal or distal margin of the tumor. Eight fiducials in eight patients were inserted in the superficial mucosal layer as noted endosonographically, necessitating repeat placement of fiducials into the muscularis propria layer during the same procedure. Only two fiducials in two patients migrated as noted during IGRT. One patient had post-procedure bleeding which was not related to fiducial placement but was due to migration of an esophageal stent that was placed at the time of fiducial placement.

Gastroesophageal junction cancer

Thirty-three patients with gastroesophageal junction (GEJ) tumors had 57 (5.2 %) fiducials placed. Fiducials were placed at both the proximal and distal margins of the tumor in 21 patients (63.6 %) and in 12 patients (36.4 %) only one fiducial was directly placed proximal to the tumor due to inability to traverse the tumor with the echoendoscope.

Table 2 Results.

Tumor location	Patients	No. fiducials placed	Technical difficulty (no. of cases)	Technical success (%)	Fiducial migration (no. of cases)	Adverse events
Esophageal	207	348 (32 %)	8 (1.5 %) placed into superficial layers repeated to place into muscularis layer	207 (100 %)	2 (0.4 %) noted during planning CT scan.	0
GE junction	33	57 (5.3 %)	0	33 (100 %)	0	0
Pancreatic	188	510 (46.7 %)	16 (3 %) due to intervening vessels	187 (99.5 %) No fiducials placed due to intervening blood vessels in one.	2 (0.4 %) noted during the endoscopy procedure 1 (0.2 %) unraveling occurred inside the tissue	7 minor[1] bleeding
Rectal	54	103 (9.3 %)	1 (0.2 %)	54 (100 %)	0	1 minor[1] bleeding
Others	32	75 (6.7 %)	2 (0.4 %) fiducials slipped out 1 (0.2 %) needle changed from 19 to 22 gauge	32 (100 %)	2 (0.4 %) needle changed from 22 to 19 gauge	1 minor[1] bleeding
Total	514	1093	29 (5.6 %)	513 (99.8 %)	7 (1.4 %)	9 (1.8 %)

No., number CT, computed tomography
[1] Spontaneously resolved bleeding

Pancreatic cancer

One hundred and eighty-eight patients with pancreatic cancer had 510 (46.7 %) fiducials placed. A 22-gauge needle was used to place 414 (81.2 %) 0.35 × 10 mm fiducials in 150 patients (80 %), a 19-gauge needle was used to place 93(18.2 %) 0.75 × 10 mm fiducials in 37 patients (19.7 %), and 3 (0.6 %) fiducials, size unknown, were placed in one patient (0.3 %).

Technical difficulty due to intervening blood vessels was noted in 16 patients (3.1 %). Minor bleeding that resolved spontaneously was noted in seven patients (1.3 %). Intraprocedural fiducial migration was noted in two patients (0.4 %). The EUS needle was changed from 22- to 19-gauge in two patients (0.4 %). Unraveling of the fiducial occurred after deployment into the lesion in one patient (0.1 %).

Rectal cancer

Fifty-four patients with rectal cancer had 103 (9.3 %) fiducials inserted. In 38 patients (70.3 %), fiducials were placed at both the proximal and distal margins of the lesion, nine (16.6 %) at the proximal margin only, and seven (13.1 %) at the distal margin only. A small amount of bleeding was noted which resolved spontaneously in one patient (0.2 %). Technical difficulty was also noted only in one patient (0.1 %).

Other lesions

In 32 patients, 75 fiducials were put into a variety of targets including peripancreatic and pancreatic metastatic lesions (8), mediastinal lymph nodes (6), metastatic liver lesions (6), anal canal cancers (3) and porta hepatis lymph nodes (2). Technical difficulty was noted in placing fiducials into a liver lesion in one patient (0.1 %). Two fiducials slipped while they during placement into the gastrohepatic ligament and porta hepatis lymph node. There was small self-limited bleeding noted in one patient (0.1 %) in which a fiducial was placed into a subcarinal lymph node.

Discussion

EUS-guided fiducial marker placement is becoming more widespread as more radiation oncologists are requesting placement prior to initiating IGRT. This large retrospective series clearly demonstrates that EUS-guided fiducial marker placement is safe, technically feasible, and, in addition, does not require the use of fluoroscopy. Several other groups have reported on techniques and success rates for EUS-guided fiducial marker implantation for various malignancies including pancreatic cancers [2, 3, 5 – 8], mediastinal cancers [4, 9], prostate cancer [10], cholangiocarcinoma [4], esophageal cancers [6, 11], gastric cancers [12] and metastases from a variety of primary cancers [4, 10]. Few of these reports, though, have focused on the technical aspects of EUS-guided fiducial implantation using different size needles and techniques of EUS-guided fiducial placement [13 – 16], and all the prior studies had fewer than 100 study patients (**Table 3**).

In our study, we describe fiducial marker placement in many different targets using different gauge needles and fiducial marker sizes. Minimal data or only case reports have been published regarding some of these target areas. As mentioned earlier, EUS-guided fiducial placement was possible in both proximal and distal aspects of rectal tumors in 70.3 % of cases. Our study is only the second one to report EUS-guided fiducial placement in rectal tumors, the first being reported by Moningi et al [17] albeit with only 11 patients. We also noted that in the majority of our esophageal malignancies (90.8 %), a 19-gauge needle was used for placing the 0.75 × 10 mm fiducials, which was in accordance with the study by Kashab et al [16]. However, a 22-gauge needle back loaded with 0.35 × 10 mm fiducials was used in the majority of primary pancreatic lesions (80 %) at our center. This was the preference of the endoscopists because of our experience with technical difficulty in using the 19-gauge needle in the duodenal bulb and second portion of the duodenum. This is in contrast to the majority of the prior studies published where a 19-gauge needle was used for pancreatic lesions [3, 5, 7 – 9, 16].

With regard to technical success rates, in current published series they have varied between 85 % to 100 %. [4 – 9, 14, 16] In our series of 514 patients, our success rate was 99.8 %, suggesting that EUS-guided fiducial placement in various gastrointestinal malignancies can be performed routinely with a high success rate.

Although many centers and most published series report the use of fluoroscopy to aid in EUS- guided fiducial marker placement to improve the spatial geometry of the fiducials being placed, it is unclear whether using fluoroscopy for this purpose has any impact on the clinical success rate of IGRT in these patients. In a study by Majumder et al [18] they found that achieving Ideal Fi-

Table 3 Summary of all studies on Endoscopic Ultrasonography-Guided Fiducial Placement in Gastrointestinal Malignancies including the current study.

Study	Type of study	No. of cases	Needle used, gauge	Type of fiducials (length, diameter, mm)	Technical success (%)	Adverse events related to fiducial placement (no. of cases)
Pishvaian et al (2006) [9]	P	13	19	Gold (3 or 5 × 0.8)	11 (85)	Cholangitis (1)
Varadarajulu et al (2010) [5]	R	9	19	Gold (5 × 0.8)	9 (100)	None
Park et al (2010) [7]	P	57	19	Visicoil (2.5 × 0.8)	56 (98)	Minor bleeding (1)
Sanders et al (2010) [8]	P	51	19	Gold (5 × 0.8)	46 (90)	Mild pancreatitis (1)
DiMaio et al (2010) [12]	R	30	22	Visicoil (10 × 0.35)	29 (97)	Fever (1)
Ammar et al (2010)[4]	C	13	22	Visicoil (10 × 0.35)	13 (100)	None
Khasab et al (2012) [14]	R	29 10	19 22	Gold (5 × 0.8) Visicoil (10 × 0.35)	39 (100)	None
Fernancdez et al (2013) [6]	R	60	19 22	Visicoil (10 × 0.75) Visicoil (10 × 0.35 or 10 × 0.5)	60 (100)	None
Choi et al (2014) [2]	R	32	19	Gold (3 × 0.8)	32 (100)	Mild pancreatitis (1)
Chandran et al (2014) [11]	P	8	19	Visicoil (10 × 0.35)	7 (88)	None
Moningi et al (2015) [15]	R	11	19	Gold (5 × 0.8) and X-mark fiducials (10, 20, or 30 × 0.85)	11 (100)	None
Machiels et al (2015) [12]	P	30	22	Visicoil (10 × 0.35) Cook Preloaded-Fiducial needle Hydrogel Marker	30 (100 %)	Pneumothorax (1) Mediastinitis (2)
Current study	R	514	19,22	Visicoil(10x0.35 or 0.75)	513 (99.8)	Minor bleeding(9)

P, prospective; R, retrospective; C, case series; No., number

ducial Geometry (IGF) was not necessary when placing fiducials into the pancreas for successful tracking and delivery of radiation. The ability to performing these procedures without needing fluoroscopy has inherent advantages of less procedure time, lack of radiation exposure, and flexibility to perform in endoscopy suites that lack fluoroscopy

At our institution, we measure clinical success by the increased rate of pathologic complete response (pCR) that we have observed in our esophageal cancer population since incorporation of fiducial markers and the attendant improved precision with personalized motion management and daily IGRT. In a presentation at the national ASTRO meeting in 2012 [19], we demonstrated that our technique of preoperative dose painting IMRT with fiducial markers to 56 Gy doubles the pCR without increasing toxicity. In this retrospective study, the pCR rate was 30.2 % in the 43 patients who received 50.4 Gy compared with a 60.7 % pCR rate in the 28 patients who received 56 Gy using fiducial markers without associated higher toxicity. Whether this translates into improved overall survival is still unclear as we will need a higher number of patients and longer-term follow-up to confirm these findings. We also note our center's high rate of complete (R0) resection for borderline resectable pancreatic cancer, with 51 % patients with borderline resectable pancreatic cancer undergoing resection with an R0 rate of 96 %) [20]. The fiducial markers allow the focal dose escalation of a higher dose (typically 35 – 40 Gy in 5 fractions) to the tumor/vessel abutment while the remainder of the target receives 30 Gy in 5 fractions given the adjacent gastrointestinal luminal structures. The fiducial markers facilitate the precise delivery of the high-dose region to the vascular abutment to facilitate margin negative resection while ensuring that the adjacent stomach and duodenum do not receive the high dose.

At Moffitt, our treatment pathway requires at least three fiducials in the pancreas and fiducial placement at both proximal and distal margins of luminal tumors if feasible. In cases in which proximal/distal fiducials could not be placed in esophageal/GEJ cancers due to luminal obstruction or when they were placed directly into the bulk of the tumor, that did not adversely affect the radiation treatment planning. For radiation treatment targeting, our center defines the gross tumor volume (GTV) and then an elective clinical target volume (CTV) [21]. Placement of the fiducial marker in the center of the tumor allowed us to correlate the length of the tumor with the endoscopic report and then measure the respiratory-associated target motion and ensure that the fiducial was encompassed in the region of interest every day as part of the IGRT. There would not be any difference in dose because the inferior CTV expansion is 3 to 5 cm below the inferior extent of GTV. Our radiation oncologists correlate the EUS report with the positron emission tomography/CT report and any intravenous contrast CT scan to ensure that all sites of disease (including lymph nodes) are encompassed within the target volume. For patients with esophageal cancer who receive only one fiducial, this is helpful for identification of motion management strategies to personalize the simulation parameters and for daily IGRT if we are dose-escalating the primary tumor. For example, at our institution, we dose-escalate the region demarcated as the gross tumor volume by the fiducial markers to 56 GY in 28 fractions while the remainder of the elective adjacent volume receives 50.4 in 28 fractions. Aligning the image generated on the treatment machine to the fiducial marker allows us to reliably treat the highest risk area every day and avoids potential underdosage issues [22].

Our adverse event [AE] rate of 1.8 % is not dissimilar to previous published reports in which AEs related exclusively to fiducial placement were reported during 1.7 to 7.6 % of procedures [3, 4 – 9, 14, 16]. The fiducial migration rate during planning CT was only 0.4 % and in the majority of patients in this series, migrate occurred within 48 hours after placement. Although we do not have long-term fiducial retention rates on all the patients in this study, we do have some data on esophageal cancer fiducial retention that our group reported in 2013 [23]. We published our experience in 60 patients with 105 fiducials for esophageal/GEJ cancers and confirmed stability, with 88 % still present on the post-treatment imaging films at a median of 107 days. This high retention rate, we feel, is mainly due to the placement of the fiducials into the muscularis propria next to the tumor instead of into the tumor itself. This avoids the potential for migration if the tu-

mor shrinks or completely resolves and thus, the fiducial would just pass luminally. Although no major AE such as life-threatening bleeding or death were noted in any of the prior studies or in the current study, care must be employed when performing EUS-guided fiducial placement to avoid intervening blood vessels and to ensure placement into the proper target tissue.

Limitations of this study include the retrospective nature. In addition, all procedures were performed by expert interventional endoscopists with a high volume of fiducial cases. Thus, our success rate and low AE rate may not be reproducible in the community setting.

Conclusions

This large retrospective study demonstrates that EUS-guided fiducial marker placement without the aid of fluoroscopy is technically safe and feasible in patients undergoing IGRT for various gastrointestinal malignancies. We expect that the indications and requests for EUS-guided fiducial marker placement will continue to increase in the future as fiducial markers allow radiation oncologists to more confidently demarcate the local extent of disease and to quantify the location of a tumor as it moves with respiration, thereby allowing dose escalation to the tumor. This improves the therapeutic ratio of higher dose to the target while not compromising normal tissue morbidity. The added knowledge that fiducials can be placed without fluoroscopy may allow for more widespread adoption of this technique in endoscopy settings where simultaneous EUS and fluoroscopy are not readily available.

Competing interests: None

References

1 *Chang BW*, *Saif MW*. Stereotactic body radiation therapy (SBRT) in pancreatic cancer: is it ready for prime time? JOP 2008; 9: 676 – 682
2 *Kothary N*, *Dieterich S*, *Louie JD* et al. Percutaneous implantation of fiducial markers for imaging-guided radiation therapy. AJR Am J Roentgenol 2009; 192: 1090 – 1096
3 *Jun-Ho Choi*, *Dong-Wan Seo*, *Do Hyun Park* et al. Fiducial placement for stereotactic body radiation therapy under only endoscopic ultrasonography guidance in pancreatic and hepatic malignancy: practical feasibility and safety. Gut Liver 2014; 8: 88 – 93
4 *Ammar T*, *Coté GA*, *Creach KM* et al. Fiducial placement for stereotactic radiation by using EUS: feasibility when using a marker compatible with a standard 22-gauge needle. Gastrointest Endosc 2010; 71: 630 – 633
5 *Varadarajulu S*, *Trevino JM*, *Shen S* et al. The use of endoscopic ultrasound-guided gold markers in image-guided radiation therapy of pancreatic cancers: a case series. Endoscopy 2010; 42: 423 – 425
6 *Fernandez DC*, *Hoffe SE*, *Barthel JS* et al. Stability of endoscopic ultrasound-guided fiducial marker placement for esophageal cancer target delineation and image-guided radiation therapy. Pract Radiat Oncol 2013; 3: 32 – 39
7 *Park WG*, *Yan BM*, *Schellenberg D* et al. EUS-guided gold fiducial insertion for image-guided radiation therapy of pancreatic cancer: 50 successful cases without fluoroscopy. Gastrointest Endosc 2010; 71: 513 – 518
8 *Sanders MK*, *Moser AJ*, *Khalid A* et al. EUS-guided fiducial placement for stereotactic body radiotherapy in locally advanced and recurrent pancreatic cancer. Gastrointest Endosc 2010; 71: 1178 – 1184
9 *Pishvaian AC*, *Collins B*, *Gagnon G* et al. EUS-guided fiducial placement for CyberKnife radiotherapy of mediastinal and abdominal malignancies. Gastrointest Endosc 2006; 64: 412 – 417
10 *Yang J*, *Abdel-Wahab M*, *Ribeiro A*. EUS-guided fiducial placement after radical prostatectomy before targeted radiation therapy for prostate cancer recurrence. Gastrointest Endosc 2011; 73: 1302 – 1305
11 *Chandran S*, *Vaughan R*, *Efthymiou M* et al. A pilot study of EUS-guided fiducial insertion for the multidisciplinary management of gastric cancer. Endosc Int Open 2014: 2 E153 – 159
12 *Machiels M*, *Hooft Jv*, *Jin P* et al. Endoscopy/EUS-guided fiducial marker placement in patients with esophageal cancer: a comparative analysis of 3 types of markers. Gastrointest Endosc 2015; 82: 641 – 649
13 *Ghassemi S*, *Faigel DO*. EUS-guided placement of fiducial markers using a 22-gauge needle. [Abstract] Gastrointest Endosc 2009; 69: AB337 – AB338
14 *DiMaio CJ1*, *Nagula S*, *Goodman KA* et al. EUS-guided fiducial placement for image-guided radiation therapy in GI malignancies by using a 22-gauge needle. Gastrointest Endosc 2010; 71: 1204 – 1210
15 *Owens DJ*, *Savides TJ*. EUS placement of metal fiducials by using a backloaded technique with bone wax seal. Gastrointest Endosc 2009; 69: 972 – 973
16 *Khashab MA*, *Kim KJ*, *Tryggestad EJ* et al. Comparative analysis of traditional and coiled fiducials implanted during EUS for pancreatic cancer patients receiving stereotactic body radiation therapy. Gastrointest Endosc 2012; 76: 962 – 971
17 *Moningi S*, *Walker AJ*, *Malayeri AA* et al. Analysis of fiducials implanted during EUS for patients with localized rectal cancer receiving high-dose rate endorectal brachytherapy. Gastrointest Endosc 2015; 81: 765 – 769
18 *Majumder S*, *Berzin TM*, *Mahadevan A* et al. Endoscopic Ultrasound-Guided Pancreatic Fiducial Placement- How Important is Ideal Fiducial Geometry? Pancreas 2013; 42: 692 – 695
19 *Shridhar R*, *Chuong MD*, *Weber J* et al. Preoperative Dose Painting IMRT Chemoradiation to 56 Gy in Esophageal Cancer Doubles Pathologic Complete Response Rate without Increasing Toxicity. ASTRO 2012; 84: S42 (http://dx.doi.org/10.1016/j.ijrobp.2012.07.320)
20 *Mellon EA*, *Hoffe SE*, *Springett GM* et al. Long-term outcomes of induction chemotherapy and neoadjuvant stereotactic body radiation therapy for borderline resectable and locally advanced pancreatic cancer. Acta Oncol 2015: 1 – 7
21 *Gao SJ*, *Qiao X*, *Wu F* et al. Pathological Analysis of Clinical Target Volume Margin for Radiotherapy in Patients with Esophageal and Gastroesophageal junction cancer Int. J. Radiation Oncology Biol. Phys 2007; 67: 389 – 396
22 *Bouchard M*, *McAleer MF*, *Starkchall G*. Impact of Gastric Filling on Radiation Dose Delivered to Gastroesophageal junctions tumors. J. Radiation Oncology Biol. Phys 2010; 77: 292 – 300
23 *Fernandez DC*, *Hoffe SE*, *Barthel JS* et al. Stability of endoscopic ultrasound-guided fiducial marker placement for esophageal cancer target delineation and image-guided radiation therapy. Pract Radiat Oncol 2013; 3: 32 – 39