Received:
11 October 2013

Revised:
4 April 2014

Accepted:
14 April 2014

doi: 10.1259/bjr.20130642

Cite this article as:

Yu Y-P, Yu Q, Guo J-M, Jiang H-T, Di X-Y, Zhu Y. Effectiveness and security of CT-guided percutaneous implantation of ^{125}I seeds in pancreatic carcinoma. *Br J Radiol* 2014;87:20130642.

FULL PAPER

Effectiveness and security of CT-guided percutaneous implantation of ^{125}I seeds in pancreatic carcinoma

¹Y-P YU, ²Q YU, ³J-M GUO, ¹H-T JIANG, ¹X-Y DI and ¹Y ZHU

¹Department of Radiology, Zhejiang Cancer Hospital, Hangzhou, Zhejiang, China

²Department of Oncological Surgery, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang, China

³Department of Abdominal Surgery, Zhejiang Cancer Hospital, Hangzhou, Zhejiang, China

Address correspondence to: Dr Yan-Ping Yu

E-mail: yuyanpingyuyu@hotmail.com

Objective: To assess the effectiveness and security of CT-guided percutaneous implantation of iodine-125 (^{125}I)-labelled seeds in pancreatic carcinoma.

Methods: A total of 36 patients (25 males and 11 females) with an average age of 57 years (range, 39–84 years) were enrolled and categorized into Stage III (27 cases) and Stage IV (9 cases) of pancreatic cancer. There were 3 tumours in the pancreatic head and 33 tumours in the pancreatic body or tail. The average diameter of the tumours was 37.1 mm (range, 15–65 mm). The implantation of ^{125}I seeds was performed by using 18-G needles (length, 150–200 mm) through the anterior, lateral and posterior approaches. Then, ^{125}I seeds were loaded and released into the lesions.

Results: Implantations were performed via the anterior (23 patients), lateral (9 patients) and posterior (4 patients) approaches. During implantation, 3–14 punctures were performed for each patient, and a total of 164

punctures were recorded. Meanwhile, a total of 657 seeds were implanted with an average of 25.27 (range, 12–50) seeds per patient, and the success rate was 100%. The activity of each seed ranged from 0.55 to 0.65 mCi. A main adverse event occurred in one puncture and minor events in seven punctures. No significant relationship between the punctures or adverse events was identified. No serious complication was detected after the implantations during follow-up visits.

Conclusion: This study suggested that CT-guided percutaneous implantation of ^{125}I seeds in a pancreatic carcinoma was relatively safe and effective for treating unresectable pancreatic cancer.

Advances in knowledge: The CT-guided percutaneous implantation of ^{125}I seeds in unresectable pancreatic cancer showed highly successful rates without serious complications.

Pancreatic cancer is the sixth most common cause of cancer-related deaths in China and the fourth worldwide.¹ The life quality of a patient with pancreatic cancer is severely influenced, since pancreatic cancer develops rapidly and can lead to abdominal pain, weight loss and jaundice.² Clinically, early pancreatic cancer does not cause obvious symptoms, while the later symptoms are usually non-specific and varied.³ As a result, most patients are diagnosed with mid- and terminal-staged pancreatic cancer that cannot be removed surgically. Although 15–20% of patients are diagnosed at an early stage, only 20–25% of them may survive more than 5 years after a tumour resection.⁴ For all stages of pancreatic cancer, the 5-year relative survival rate is 6%, whereas the 5-year survival rate is approximately 15% for a local tumour.⁵ Local control and distant metastases are the major factors that affect prognoses.⁶ During the past decades, the treatment outcome of locally advanced pancreatic carcinoma has not been improved significantly.⁷

Currently, comprehensive therapy (radiotherapy plus chemotherapy) is the most common treatment for locally advanced pancreatic carcinoma.^{8,9} Radioactive seeds, interstitial brachytherapy¹⁰ and conformal radiotherapy,⁷ show great curative effects on local control. The implantation methods include intra-operative and ultrasound- and CT-guided implantations.^{10–12}

With the development of modern medical imaging technology, the CT-guided percutaneous implantation technique has been widely applied in clinics.^{12,13} Additionally, CT-guided implantation of iodine-125 (^{125}I)-labelled seeds shows precision position, minimal invasion and great effectiveness. Also, the slow and continuous release of ^{125}I seeds has been radiobiologically advantageous, allowing the repair of non-lethal damage and re-oxygenation of hypoxic areas in normal tissues.⁷ However, the security of percutaneous implantation guided by CT scanning is still contradictory, because the pancreas is surrounded by the liver, stomach, intestines, spleen, kidney and blood vessels.

In this present study, we retrospectively analysed 36 cases with unresectable pancreatic carcinoma who underwent CT-guided percutaneous implantation of ^{125}I seeds. The security of CT-guided percutaneous implantation of ^{125}I seeds in pancreatic carcinoma was assessed, which might provide the basis for individual treatment of CT-guided percutaneous implantation.

METHODS AND MATERIALS

Patients

From March 2009 to March 2013, in the Tumour Hospital of Zhejiang Province, China, 36 consecutive patients with unresectable pancreatic carcinoma who underwent CT-guided percutaneous implantation of ^{125}I seeds were included in this retrospective study. The criteria for enrolment included (1) adenocarcinomas of the pancreas that were pathologically diagnosed by using CT-guided fine needle aspiration before implantation;¹⁴ (2) patients in Stage III or Stage IV, according to the International Union Against Cancer (UICC) 2002 staging criteria;¹⁵ and (3) Karnofsky physical scores (KPS) ≥ 60 . In addition, patients with severe cardiopulmonary dysfunction, advanced cachexia or diameters of tumours ≥ 7 cm were excluded.

Informed consent was obtained from all patients. The whole study was approved by the Ethics Committee of the Tumour Hospital of Zhejiang Province, China.

Puncture approach and multipunctures

The three puncture approaches, including the anterior, lateral and posterior approaches, were visualized (Figure 1). Briefly, two straight lines were drawn separately from the centre of the spinal vertebral body towards the two sides of the body surface 45° from the horizontal line. The approach through the inboard region of the intersections of three straight lines was defined as the anterior approach, whereas that through the two outboard regions was defined as the lateral approach. The approach through the region between the lateral margin of the spinal column and the inside edge of the kidney was defined as the posterior approach. When a needle was repeatedly inserted into lesions in different directions, it was defined as multipunctures using one needle (Figure 2a).

Pre-operative preparation

The blood routine and blood coagulation were examined 1–3 days before the implantation of ^{125}I seeds to exclude haemorrhagic disorders. The upper-abdomen routine enhanced CT scan was performed pre-operatively. Laxatives were given in the afternoon and a liquid diet was allowed at dinner, 1 day pre-operatively. Patients fasted the following morning before the operation. Sufficient breath training was conducted to ensure normal breathing during the surgical procedure.

CT-guided percutaneous implantation protocol

For adopting the anterior, posterior and lateral puncture approaches, patients were generally in the supine position, prone position and supine, lateral or left/right anterior oblique position, respectively.

The vascular interventional catheters were located in the skin surface of the lesion site and tied at intervals of 1 cm. Based on

Figure 1. The schematic diagram of three puncture approaches. (A) A horizontal line through the centre of the spinal vertebral body; (B, C) two straight lines that were drawn separately from the centre of the spinal vertebral body towards the two sides of the body surface 45° from the horizontal line; (E, F) straight lines tangent to the lateral margin of the spinal column; (D, G) straight lines tangent to the inside edge of the kidney; (a) pancreas; (b) stomach; (c) liver; (d) kidney; (e) spleen; (f) inferior vena cava; (g) aorta abdominalis; (I) the anterior approach; (II) the lateral approach; and (III) the posterior approach.

observations via the CT scanner (GE BrightSpeed Series; GE Healthcare, Waukesha, MI) under the conditions of 120 kV and 60 mAs with a width of 5 mm and an interlamellar space of 0 mm, the lesion regions were confirmed, labelled, routinely disinfected and locally anesthetized (2% lidocaine, 3 ml). According to the puncture approach and tumour size, the number and direction angle of the needles (18-G; length, 150–200 mm; Dr Japan Co., Ltd, Tokyo, Japan) were calculated. The interval of each needle was approximately 1 cm. Based on the treatment planning system manufactured by the Fudan University, Shanghai, China,¹⁶ the needles were implanted into a pancreatic tumour with calculated depth and angle of direction. Then, ^{125}I seeds (Jaco Pharmaceutical Co., Ltd, Zhejiang, China) were loaded and released every 5- to 10-mm apart on withdrawing the needles. The ^{125}I produces γ -rays with an activity of 0.55–0.65 mCi, a radiological dose rate of 0.05–0.10 Gy h^{-1} , a half-life of 59.6 days and an effective radius of 1.72 cm. During the implantation, puncturing important visceral organs and macro-vasculature should be avoided.

In principle, as few as possible needles were used, and multipunctures with one needle were performed for smaller lesions. The whole implantation was performed under CT guidance to avoid puncturing the aorta and other main vessels. Posterior puncture approach was proposed when tumours occurred in the abdominal aorta and/or vena cava. The procedure was performed for approximately 120–180 min in the CT room. The path of the needles was monitored for haemorrhages. All patients underwent an immediate post-procedure CT scan to identify the implantation of the seeds.

Figure 2. Three puncture approaches of implantation in a pancreatic carcinoma. (a) Percutaneous implantation with multineedle-punctured pancreas via the anterior approach; (b) percutaneous implantation with single-needle-punctured stomach via the anterior approach; (c) percutaneous implantation with single-needle-punctured intestines via the lateral approach; (d) percutaneous implantation with single needle via the posterior approach.

Definition of security

In this study, the security of an implantation was evaluated according to the following aspects: adverse events, including main and minor clinical events; and the toxicity of ^{125}I seed implantation.

The main clinical events included (1) haemorrhage, haematemesis and progressive haematochezia (the bleeding volume $>50\text{ ml}$); (2) acute pancreatitis or pancreatic fistula; and (3) gastrointestinal perforation. The minor clinical events included (1) no bleeding or the bleeding volume $<50\text{ ml}$ in the needle-path; and (2) a positive faecal occult blood test (FOBT) or melaena within 24 h after operation without other symptoms.

Post-operative treatment and follow-up visit

Routinely, the compression on the surface of the puncture region was maintained for 10 min. If a haemorrhage in the path of the needles occurred, the compression time was extended to 30 min to achieve haemostasis. Then, the implantation puncture site was bandaged. Outpatients were kept in the hospital for 2 h. All patients were followed up for about 2 months after the implantation to examine the complications or adverse events.

Statistical analysis

The data were analysed using the SPSS® v. 16.0 software (SPSS Inc., Chicago, IL). The probabilities of complications among the

different approaches were calculated and tested by χ^2 test. A p -value <0.05 was considered statistically significant.

RESULTS

Clinical characteristics of patients

A total of 36 patients with pancreatic cancer were enrolled, including 25 males and 11 females, with an average age of 57 years (range, 39–84 years). According to the UICC 2002 staging criteria,¹⁵ 27 cases were at Stage III and 9 cases at Stage IV of pancreatic cancer. The main clinical manifestations were epigastric discomfort, abdominal pain and jaundice. 3 patients had a tumour in the pancreatic head and 33 had a tumour in the pancreatic body or tail. The average diameter of the tumours was 37.1 mm (range, 15–64 mm). The KPS of 2 patients were 60–70, of 8 patients were 70–80 and of 26 patients were >80 . The jaundice indexes of three patients with pancreatic head tumours were increased up to 3.6 times the normal values, while liver function, blood routine examinations and routine urine tests of the other patients were normal.

Puncture approaches

There were 23 patients who received surgery through the anterior approach (Figure 2a,b), 9 patients through the lateral approach (Figure 2c) and 4 patients through the posterior approach (Figure 2d). The number of implanted ^{125}I seeds ranged from 12 to 50 in each patient with an average of 25.27. A total of 657 ^{125}I seeds were implanted in the 36 patients. Specific activity of

Table 1. The analysis of adverse events during implantation

Organs	Patients (<i>n</i> = 36)	Punctures (<i>n</i> = 164)	Adverse events	
			Main event	Minor event
Normal visceral organs	17	84		2
Punctured visceral organs	19	80	1	5
Liver	4	18		
Stomach	8	33	1	1
Intestines	7	29		4

each seed ranged from 0.55 to 0.65 mCi, and the success rate was 100%.

Punctured visceral organs and complications

During the implantation, the visceral organs of 19 patients were punctured, including the liver (4 cases), stomach (8 cases) and intestines (7 cases). These 19 patients displayed one main adverse event and five minor events (Table 1).

For the four liver-punctured patients, a total of 18 punctures were performed with an average of 4.5 (range, 3–6) punctures per patient, and no obvious haemorrhage or other adverse events were observed (Figure 3a, Table 1).

For the 8 stomach-punctured cases, a total of 33 punctures were performed with an average of 4.13 (range, 3–11) punctures per patient, and one main adverse event and one minor event occurred (Table 1). The main event was massive bleeding of the alimentary tract (>500 ml) 3 days after the implantation of 20

¹²⁵I seeds (activity of 0.6–0.8 mCi and dose of 140 Gy), which was caused by cancerous ulcers owing to the invasion of the gastric wall by the pancreatic tumour, and was treated via emergency exploratory laparotomy (Figure 3b). The minor event was slight bleeding of the gastric wall (<20 ml) during implantation.

Also, among the seven intestine-punctured cases, a total of 29 punctures were performed with an average of 4.14 (range, 3–7) punctures per patient, and four minor adverse events occurred with slight bleeding (<20 ml) and without clinical responses (Figure 2c, Table 1). The incidence rates of the minor events were not statistically different among liver-, stomach- and intestine-punctured patients ($\chi^2 = 4.600$; $p = 0.100$).

Meanwhile, the puncturing of the visceral organs was successfully avoided in 17 patients, and a total of 84 punctures showed two minor adverse events, including one slight bleeding in the

Figure 3. The punctured visceral organs during implantation. (a) The punctured liver without obvious haemorrhage or other adverse events. (b) The punctured stomach with a cancerous ulcer due to gastric wall invasion by pancreatic tumour (indicated by arrow). (c) The needle punctured a 3-mm-diameter vessel (indicated by arrow). (d) Slight bleeding when withdrawing the needle from the mesenteric small blood vessels (indicated by arrow).

Table 2. The relationship between the number of punctures and adverse events

Punctures per patient	Total punctures	Adverse events	
		Minor events	Main event
≤4	69	4	0
≥5	95	3	1

path of the needle (<10 ml) and one bleeding while withdrawing the needle from the mesenteric small blood vessels (<5 ml) (Figure 3c,d).

Neither the main events nor the minor events were statistically different between the 17 patients without punctured visceral organs and the 19 patients with punctured visceral organs ($p = 0.528$ and 0.271 , respectively). Additionally, there was no significant difference in the main events and minor events between 84 punctures (17 patients without punctured visceral organs) and 80 punctures (19 patients with punctured visceral organs) ($\chi^2 = 1.056$; $p = 0.304$ and $\chi^2 = 1.501$; $p = 0.220$, respectively).

Among all the 164 punctures in the 36 patients, 69 punctures performed in patients with 3–4 punctures showed four minor adverse events, whereas 95 punctures performed in patients with 5–14 punctures showed one main adverse event and three minor events (Table 2). No statistical difference was found between the adverse events of these two groups ($\chi^2 = 0.681$; $p = 0.409$).

Additionally, in one case, the ¹²⁵I seeds were wrongly implanted into the gastric wall owing to unsuccessful breathing control of the patient, and the tumour was close to the gastric wall. However, no migration to other tissues was detected under CT scanning of the whole abdomen (Figure 4).

There was no serious complication detected after implantation in all cases, such as abdominal pain, pneumoperitoneum or gastrointestinal tract perforation. No patient died owing to the implantation of ¹²⁵I seeds.

Follow-up visit

All patients showed negative FOBT within 24 h after implantation. Slightly increased hemodiastase in one case returned to the normal level, 3 days after the implantation.

Within the first week after implantation, three patients showed intermittent abdominal pain with a normal serum amylase level and without fever. The symptom of intermittent abdominal pain disappeared 1 week after the implantation without any special treatment. During the follow-up visit, other symptoms, such as pancreatitis, pancreatic fistula and pancreatic pseudocyst, were not detected.

One seed was wrongly implanted into the gastric wall of one patient. A 6-month follow-up visit of this patient showed no severe complication because of the low dosage of the single seed (0.6 mCi) and the thick gastric wall.

DISCUSSION

The survival rate of patients with pancreatic cancer remains low, although various therapeutic modalities have been applied.¹⁷ The 5-year survival rate is <10% after radiation therapy with or without chemotherapy.¹⁸ Most patients are diagnosed with advanced pancreatic cancer, and the management of which is still controversial.¹² Our previous study¹³ had shown that the tumour response rate of chemotherapy combined with the implantation of ¹²⁵I seeds and of chemotherapy combined with radiotherapy in locally advanced pancreatic cancer was, respectively, 73.33% (11/15) and 26.67% (4/15), and the median survival time was 14 [95% confidence interval (CI), 13.215–14.785 months] and 12 months (95% CI, 10.884–13.116 months), respectively, during the 3-year follow-up. The toxicity of the implantation of ¹²⁵I seeds was lower than that of radiotherapy in the pancreas. According to the National Comprehensive Cancer Network 2013 clinical practice guidelines for pancreatic cancer (www.tri-kobe.org/nccn/guideline/pancreas/english/pancreatic.pdf), the recommended dose of post-operative radiotherapy with and without tumour resection is 45–54 Gy and 50–60 Gy, respectively. However, the implantation of ¹²⁵I seeds shows sustained radiation with a half-life of 60 days and a radiation radius of 1.72 cm. The recommended dose of seed implantations is 2–3 times that of radiotherapy. Currently, CT-guided percutaneous implantation of ¹²⁵I seeds may be an alternative in the treatment of local

Figure 4. The iodine-125 seeds were wrongly implanted into the gastric wall in one case (indicated by arrow).

pancreatic cancer. However, the security of this procedure is contradictory because of the complex anatomical relationship of the visceral organs and the damaging effects of radiation.¹⁹ Therefore, we retrospectively analysed 36 cases who underwent CT-guided percutaneous implantation of ¹²⁵I seeds at our hospital, to investigate the relationship between punctures and adverse events and to assess the security of this procedure.

In our study, an 18-G puncture needle was used and a total of 164 punctures were performed in 36 patients. A minor adverse event occurred in 7 punctures, accounting for 4.27% (7/164). Meanwhile, a major adverse event, bleeding of >100 ml during implantation, occurred during 1 puncture, accounting for 0.61% (1/164). The complication rate in our study coincides with that in the literature. Zhongmin et al¹² have revealed that 31 patients with advanced pancreatic cancer who received CT-guided ¹²⁵I seed implantation therapy have had an overall response rate of 61.3%, a local control rate of 90.3% and a pain relief rate of 92%, without serious complications during the follow-up study.

In addition, the incidence rates of complications were not statistically different between the normal visceral organs group and the visceral organs punctured group. Besides, patients with 3–4 punctures and patients with 5–14 punctures did not show a significant difference in adverse events. These results confirmed that the CT-guided ¹²⁵I seed percutaneous implantation therapy is relatively safe. Clinically, ultrasound- and CT-guided ¹²⁵I seed percutaneous implantation therapies have been utilized for targeting liver malignancies,²⁰ lung cancer²¹ and local recurrent rectal carcinoma.¹⁸ Many researchers have confirmed the

safety of this technique with a mortality rate of 0.006–0.031% and a complication rate of 0.5–3%.^{22,23} Also, implantation of ¹²⁵I seeds could destroy the residual cancer cells after cryosurgery, showing a complementary effect of ¹²⁵I seed implantation combined with cryosurgery.²⁴ Additionally, chemotherapy after the implantation of ¹²⁵I seeds could enhance the local control rates of tumours.²⁵ However, the seed implantation showed a short radial distance with radiation radius of 1.72 cm, and its dose distribution was hardly homogeneous. In conclusion, this retrospective analysis of 36 cases with unresectable pancreatic carcinoma, who underwent the CT-guided percutaneous implantation of ¹²⁵I seeds, showed 1 major event (1/164) and 7 minor events (7/164) during implantation. No significant relationship between punctures and adverse events was identified. No serious complication was detected during follow-up study. Therefore, our study suggests that the CT-guided percutaneous implantation of ¹²⁵I seeds in pancreatic carcinoma is relatively safe and effective for treating unresectable pancreatic cancer. However, a further study with a larger sample size is still needed.

ACKNOWLEDGMENTS

The authors thank Dr Qing-Hua Deng (Zhejiang Cancer Hospital, Zhejiang, China) for his great help on radiotherapy. They also appreciate the contributions and support of all the nurses and technicians at the Department of Intervention (Zhejiang Cancer Hospital, Zhejiang, China).

FUNDING

This study is supported by the Research Fund of Zhejiang Province for Medical Sciences, No. 2009B021.

REFERENCES

- Zhang L, Wu C, Zhang Y, Liu F, Zhao M, Bouvet M, et al. Anti-metastatic and survival efficacy and safety comparison of traditional Chinese medicine herbal mixture LQ versus gemcitabine in a human pancreatic cancer orthotopic nude-mouse model. *J Cell Biochem* 2013; **114**: 2131–7.
- Walsh D, Donnelly S, Rybicki L. The symptoms of advanced cancer: relationship to age, gender, and performance status in 1,000 patients. *Support Care Cancer* 2000; **8**: 175–9.
- Zhang L, Jin H, Guo X, Yang Z, Zhao L, Tang S, et al. Distinguishing pancreatic cancer from chronic pancreatitis and healthy individuals by (1)H nuclear magnetic resonance-based metabonomic profiles. *Clin Biochem* 2012; **45**: 1064–9.
- Li D, Xie K, Wolff R, Abbruzzese JL. Pancreatic cancer. *Lancet* 2004; **363**: 1049–57. doi: 10.1016/S0140-6736(04)15841-8
- Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. *CA Cancer J Clin* 2010; **60**: 277–300. doi: 10.3322/caac.20073
- Chang DT, Schellenberg D, Shen J, Kim J, Goodman KA, Fisher GA, et al. Stereotactic radiotherapy for unresectable adenocarcinoma of the pancreas. *Cancer* 2009; **115**: 665–72. doi: 10.1002/cncr.24059
- Ceha HM, van Tienhoven G, Gouma DJ, Veenhof CH, Schneider CJ, Rauws EA, et al. Feasibility and efficacy of high dose conformal radiotherapy for patients with locally advanced pancreatic carcinoma. *Cancer* 2000; **89**: 2222–9.
- Yeo CJ, Cameron JL, Lillemoe KD, Sitzmann JV, Hruban RH, Goodman SN, et al. Pancreaticoduodenectomy for cancer of the head of the pancreas. 201 patients. *Ann Surg* 1995; **221**: 721–31.
- Sultana A, Tudur Smith C, Cunningham D, Starling N, Tait D, Neoptolemos JP, et al. Systematic review, including meta-analyses, on the management of locally advanced pancreatic cancer using radiation/combined modality therapy. *Br J Cancer* 2007; **96**: 1183–90.
- Jin Z, Du Y, Li Z, Jiang Y, Chen J, Liu Y. Endoscopic ultrasonography-guided interstitial implantation of iodine 125-seeds combined with chemotherapy in the treatment of unresectable pancreatic carcinoma: a prospective pilot study. *Endoscopy* 2008; **40**: 314–20.
- Willett CG, Del Castillo CF, Shih HA, Goldberg S, Biggs P, Clark JW, et al. Long-term results of intraoperative electron beam irradiation (IOERT) for patients with unresectable pancreatic cancer. *Ann Surg* 2005; **241**: 295–9.
- Zhongmin W, Yu L, Fenju L, Kemin C, Gang H. Clinical efficacy of CT-guided iodine-125 seed implantation therapy in patients with advanced pancreatic cancer. *Eur Radiol* 2010; **20**: 1786–91. doi: 10.1007/s00330-009-1703-0
- Zhang FJ, Wu PH, Zhao M, Huang JH, Fan WJ, Gu YK, et al. CT guided radioactive seed ¹²⁵I implantation in treatment of pancreatic cancer. [In Chinese.] *Zhonghua Yi Xue Za Zhi* 2006; **86**: 223–7.
- Gupta S, Ahrar K, Morello FA Jr, Wallace MJ, Hicks ME. Masses in or around the pancreatic head: CT-guided coaxial fine-needle aspiration biopsy with a posterior transcaval approach. *Radiology* 2002; **222**: 63–9.

15. Morin E, Cheng S, Mete O, Serra S, Araujo PB, Temple S, et al. Hormone profiling, WHO 2010 grading, and AJCC/UICC staging in pancreatic neuroendocrine tumor behavior. *Cancer Med* 2013; **2**: 701–11.
16. Chen HH, Jia RE, Yu L, Zhao MJ, Shao CL, Cheng WY. Bystander effects induced by continuous low-dose-rate ^{125}I seeds potentiate the killing action of irradiation on human lung cancer cells in vitro. *Int J Radiat Oncol Biol Phys* 2008; **72**: 1560–6.
17. Abrams RA, Lowy AM, O'Reilly EM, Wolff RA, Picozzi VJ, Pisters PW. Combined modality treatment of resectable and borderline resectable pancreas cancer: expert consensus statement. *Ann Surg Oncol* 2009; **16**: 1751–6.
18. Wang Z, Lu J, Liu L, Liu T, Chen K, Liu F, et al. Clinical application of CT-guided (125)I seed interstitial implantation for local recurrent rectal carcinoma. *Radiat Oncol* 2011; **6**: 138.
19. Mohiuddin M, Rosato F, Barbot D, Schuricht A, Biermann W, Cantor R. Long-term results of combined modality treatment with I-125 implantation for carcinoma of the pancreas. *Int J Radiat Oncol Biol Phys* 1992; **23**: 305–11.
20. Zhang FJ, Li CX, Jiao DC, Zhang NH, Wu PH, Duan GE, et al. CT guided ^{125}I seed implantation for portal vein tumor thrombus in primary hepatocellular carcinoma. *Chin Med J (Engl)* 2008; **121**: 2410–14.
21. Wang ZM, Lu J, Liu T, Chen KM, Huang G, Liu FJ. CT-guided interstitial brachytherapy of inoperable non-small cell lung cancer. *Lung Cancer* 2011; **74**: 253–7. doi: [10.1016/j.lungcan.2011.03.006](https://doi.org/10.1016/j.lungcan.2011.03.006)
22. Paulsen SD, Nghiem HV, Negussie E, Higgins EJ, Caoili EM, Francis IR. Evaluation of imaging-guided core biopsy of pancreatic masses. *AJR Am J Roentgenol* 2006; **187**: 769–72. doi: [10.2214/AJR.05.0366](https://doi.org/10.2214/AJR.05.0366)
23. Smith EH. Complications of percutaneous abdominal fine-needle biopsy. Review. *Radiology* 1991; **178**: 253–8. doi: [10.1148/radiology.178.1.1984314](https://doi.org/10.1148/radiology.178.1.1984314)
24. Xu KC, Niu LZ, Hu YZ, He WB, He YS, Li YF, et al. A pilot study on combination of cryosurgery and (125)iodine seed implantation for treatment of locally advanced pancreatic cancer. *World J Gastroenterol* 2008; **14**: 1603–11.
25. Cron GO, Beghein N, Crokart N, Chavée E, Bernard S, Vynckier S, et al. Changes in the tumor microenvironment during low-dose-rate permanent seed implantation iodine-125 brachytherapy. *Int J Radiat Oncol Biol Phys* 2005; **63**: 1245–51.