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Individually optimized stereotactic radiotherapy for pancreatic head tumors: A planning feasibility study

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ABSTRACT

Aim: Aim of this study was to perform a planning feasibility analysis of a 3-level dose prescription using an IMRT-SIB technique.
Background: Radiation therapy of locally advanced pancreatic cancer should administer a minimum dose to the duodenum and a very high dose to the vascular infiltration areas to improve the possibility of a radical resection.
Materials and methods: Fifteen patients with pancreatic head adenocarcinoma and vascular involvement were included. The duodenal PTV (PTVd) was defined as the GTV overlapping the duodenal PRV. Vascular CTV (CTVv) was defined as the surface of contact or infiltration between the tumor and vessel plus a 5 mm margin. Vascular PTV (PTVv) was considered as the CTVv plus an anisotropic margin. The tumor PTV (PTVt) was defined as the GTV plus a margin including the PTVv and excluding the PTVd. The following doses were prescribed: 30 Gy (6 Gy/fraction) to PTVd, 37.5 Gy (7.5 Gy/fraction) to PTVt, and 45 Gy (9 Gy/fraction) to PTVv, respectively. Treatment was planned with an IMRT technique.
Results: The primary end-point (PTVv $D_{mean} > 90\%$) was achieved in all patients. PTVv $D_{98\%} > 90\%$ was achieved in 6 patients (40%). OARs constraints were achieved in all patients.
Conclusions: Although the PTVv $D_{95\%} > 95\%$ objective was achieved only in 40% of patients, the study showed that in 100% of patients it was possible to administer a strongly differentiated

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mean/median dose. Prospective trials based on clinical application of this strategy seem to be justified in selected patients without overlap between PTVd and PTVv.

1. Introduction

Pancreatic carcinoma is one of the neoplastic diseases with the worst prognosis. Radiation therapy has been used both as adjuvant and curative treatment. However, the ability to use effective doses is limited by the presence of the surrounding radiosensitive organs (kidney, intestine, stomach, liver, spinal cord). Hence, it is difficult to administer to the tumor a high dose of radiation. This is probably one of the reasons for the disappointing clinical results, with a median survival around 10–12 months in patients with advanced disease[1,2] and around 20–24 months in patients with resectable disease.[3]

Recently, it has been proposed by some authors to use stereotactic body radiation therapy (SBRT) for the treatment of these tumors.[4–18] The use of stereotactic techniques is theoretically useful to administer high doses of radiation to the tumor with optimum sparing of organs at risk (OARs). Furthermore, SBRT treatment has other advantages and particularly its brevity. This enables an easy integration with chemotherapy and the improvement of patients quality of life. Three recent reviews of the literature,[19–21] focused on the few experiences available in the scientific literature, highlighted that (1) treatment with radiosurgery of pancreatic tumors produces survival results similar to those recorded in series based on prolonged chemoradiation; (2) the main limitation of this technique is the high incidence of duodenal complications (bleeding, ulceration, perforation).

More recently, the possibility of administering SBRT treatments with intensity-modulated techniques (IMRT) based on the use of a Simultaneous Integrated Boost (SIB) has been proposed.[20] This method allows to simultaneously administer different doses of radiation within the target. Therefore, the use of this technique may allow the administration of a high radiation dose to the target, while delivering a reduced dose to the Planning Target Volume (PTV) subvolume overlapping the duodenal wall.[22,23]

Furthermore, several authors proposed the use of radiotherapy as preoperative treatment.[24–26] The reason is that most patients have a locally advanced and, therefore, unresectable tumor at diagnosis. Typically, the reason for unresectability is the infiltration of the blood vessels close to the pancreas (mainly the superior mesenteric artery and vein and the celiac trunk). Some studies on the use of preoperative radiotherapy and chemoradiation showed the possibility to achieve a radical resection even in patients with initially unresectable disease. However, the success rate is still low (about 25–30%)[27] because of the limits in the radiation dose that can be safely administered in this anatomical region.

In view of this problem, some authors proposed once again the use of IMRT-SIB, because of the opportunity to administer a safe dose to the PTV and a higher dose to the tumor region invading the blood vessels.[28] This technique has the potential to achieve a greater regression in this critical area of the tumor.

Both these strategies (sparing the duodenum and increasing the dose to the vessels) seem reasonable and promising. Therefore, it would be interesting to combine both of them. In fact, a combination of these dose modulations into a 3 level dose prescription can be hypothesized, with a lower dose to PTV overlapping the duodenum, a high dose to vascular invasion and an intermediate dose in the remaining PTV. However, the mean diameter of locally advanced pancreatic carcinoma being around 40–45 mm,[29] the possibility to vary the dose in such a small volume had never been hypothesized and tested in these patients.

Therefore, the aim of this study was to perform a planning feasibility analysis of a dose prescription in 3 levels within a pancreatic tumor treated by SBRT. More specifically, using the IMRT-SIB technique with 3 markedly different doses (in 5 fractions) was tested and evaluated.

2. Material and methods

2.1. Study design

A planning study was performed on a sample of 15 patients with a histologically proven pancreatic head adenocarcinoma deemed unresectable due to vascular involvement.

2.2. End-points

The primary end-point of the study was the rate of patients in whom, respecting all OARs constraints and the constraint PTVv $D_{2\%} < 115\%$, the constraint $D_{mean} > 90\%$ of the prescribed dose was achieved for the 3 different PTVs. Secondary end-points were the percentage of patients in whom, respecting all OARs constraints and the constraint PTVv $D_{2\%} < 115\%$, a PTVv near minimum dose ($D_{98\%}$) > 90%, a PTVv $D_{95\%} > 95\%$, and a median dose ($D_{50\%}$) > 95% were achieved.

2.3. Treatment simulation

The stereotactic body frame (SBF, Elekta, Crawley, UK) was used for patients immobilization. It is an immobilization device that defines a stereotactic system of coordinates for the target position instead of basing on the anatomical landmarks such as bony structures or skin markers.[30,31] To reduce involuntary abdominal movements due to respiration, an abdominal compressor is attached to the SBF by a rigid arc, aiming at minimizing the mobility of targets close to the diaphragm by mechanically pressing the patients epigastrium. Organ motion due to residual respiratory movements, resulting in target displacement, was measured by performing 30 axial CT scans on the same slice during free breathing.