

## Dose Volume Histogram (DVH) analysis of Stereotactic Body Radiotherapy (SBRT) treatment of primary pancreatic cancer: establishing risk levels for duodenal toxicity

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**Categories:** Radiation Oncology

**Keywords:** stereotactic body radiotherapy, pancreatic cancer, duodenal toxicity, dvh evaluator

### How to cite this abstract

Goldsmith C, Price P M, Cross T, et al. (June 16, 2016) Dose Volume Histogram (DVH) analysis of Stereotactic Body Radiotherapy (SBRT) treatment of primary pancreatic cancer: establishing risk levels for duodenal toxicity. Cureus 8(6): a107

## Abstract

**Objectives:** To perform dose response modelling, using robust clinical outcome data, to define risk levels for Grade 3-4 duodenal toxicity in the SBRT treatment of primary pancreatic cancer.

**Methods:** 44 patients with unresectable pancreatic tumours were treated with SBRT using robotic radiosurgery between March 2009 and March 2013 at The Harley Street Clinic, London, UK. It is standard practice at this centre to insert multiple (4+) fiducials for tracking purposes, but due to the close relationship of pancreatic tumour and surrounding Organs At Risk (OAR) this is not always possible. 41 patients were prescribed 18-36 Gy in 3 fractions (BED= 24.5-79.2, using the linear quadratic model with  $\alpha/\beta=10\text{Gy}$  for tumour control). 3 patients were prescribed 22.5-25Gy in 5 fractions as re-irradiation for their pancreatic cancer (BED10 32.6-37.5). Prior to analysing duodenal tolerance, all doses were converted to 3 fraction equivalent dose using  $\alpha/\beta=3\text{Gy}$ . Preferred planning constraints for duodenal toxicity were 24Gy maximum point dose to 0.035cc, and 16.5Gy to =5cc and 11.4Gy to =10cc, with dose escalation as experience permitted. Logistic dose response modelling was performed in the DVH Evaluator software (DiversiLabs LLC, Huntingdon Valley, Pa, USA) with maximum likelihood parameter fitting. Confidence intervals were constructed via the profile likelihood method. Toxicity and outcome data were prospectively collected at 3 months after treatment, then 6-monthly intervals thereafter. Toxicity was assessed using Common Toxicity Criteria Adverse Events version 3 (CTCAEv3).

**Results:** 32 patients had multiple fiducials and among them, two Grade 3 complications occurred that were likely due to SBRT and that correlated with duodenal dose; one duodenal haemorrhage and one duodenal stricture. The cases without multiple fiducials had increased number of complications and will be discussed separately in the presentation. Two other patients with multiple fiducials had general constitutional Grade 3 complications, one with obstructive jaundice and one with fatigue and diarrhoea. When analysed separately, these two cases with non-specific toxicity did not yield a dose response for duodenal toxicity, and these were excluded from the remainder of the analysis. For D0.035cc to the Duodenum, the resulting model parameters for duodenal haemorrhage and stricture were TD50=89.7Gy, ?50=1.0194.

### Open Access

#### Abstract

Published 06/16/2016

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Limiting the dose to the duodenum to D1cc <37.4Gy (in 3 fractions) equates to a risk level of <20% risk of Grade 3+ duodenal toxicity. Limiting the D1cc duodenal dose limit to 31.4Gy in 3 fractions is associated with a 10% risk of G3+ duodenal toxicity (this is a more clinically acceptable risk level). The DVH risk map of duodenal tolerance in 1 to 5 fractions will be displayed

Conclusions: Dose escalation in pancreatic cancer is likely to translate into improved tumour control. Clinicians are concerned about the likely toxicity of dose escalation due to surrounding critical normal tissue, and are keen to quote evidence-based estimates of toxicity risk when consenting a patient for SBRT treatment. Our DVH analysis has shown Duodenum D1cc < 31.4Gy in 3 fractions to be associated with a 10% risk level of Grade 3+ duodenal toxicity. In addition, our analysis supports the strategy to implant multiple fiducials for tracking as these cases were associated with a more favourable toxicity profile.