Executive Summary

Background

Intensity-modulated radiotherapy (IMRT) in anal cancer (AC) allows optimal dose coverage to the tumour whilst sparing normal tissues (1, 2). The genitalia are situated within close proximity to the anal tumour and the inguinal pelvic nodes which require radiotherapy treatment therefore the genitalia are difficult to avoid. Side effects include acute skin reactions and long term fibrosis, pain and sexual dysfunction (3-5).

In contrast to other normal tissues the tolerance of the genitalia exposed to radiation is not known. In order to achieve this knowledge there should be a standard genitalia contouring method in radiotherapy planning. Genitalia 'dose constraints' aimed for in an IMRT AC plan should be met ideally within a large prospective clinical trial. However until now no official guidelines existed to describe how to contour the genitalia in radiotherapy planning therefore there is large variation of genitalia contours produced. Attempts to currently analyse genitalia dose data are meaningless due to the inconsistent contouring practice. In addition current genitalia dose constraints do not appear to be evidence based and are rarely met in clinical practice. The threshold dose between genitalia irradiated to various dose levels and occurring side effects are not known.

Five-year overall survival rates are approximately 70-80% (6). Therefore quality of life following treatment for this subset of patients is important. The first step towards improving outcomes is to understand the relationship between irradiated genitalia tissue and associated side effects. In the context of radiotherapy planning this requires evaluation of current practice. Previous to this current research project a genitalia contouring atlas was devised to improve consistency of genitalia contouring between patients (7). The overall aim of this current research project is to apply the genitalia atlas to a retrospective set of AC IMRT plans and quantify the genitalia dose differences between the original genitalia contour as defined by the clinician and the new genitalia contour defined with the aid of the atlas. This study also investigated;

a) Volume differences between original and new genitalia contours.
b) Compliance of existing dose constraints for original and new genitalia contours.
c) Correlations between genitalia tissue irradiated and planning target volume size and genitalia tissue overlapping with phase 1 PTV (PTV1).
d) Dose differences in genitalia irradiation when analysed by gender and tumour stage.

By defining consistent genitalia contours the genitalia dose that was actually received can be determined. The outcome of this project was to recommend new genitalia dose constraints that are gender and tumour stage specific that can then be used for prospective radiotherapy plans and correlated with side effects seen in the clinic.

Methodology

Patient Population: Sixty patients previously diagnosed with AC and received combined modality therapy were retrospectively identified (Table 1).

Characteristic	*n*	Characteristic	*n*
Gender		*Gender*	
Male	20	Female	40
T stage		T stage	
1	2	1	4
2	5	2	17
3	5	3	10
4	8	4	9
N stage		N stage	
0	10	0	24
1	3	1	6
2	2	2	7
3	5	3	3
TNM Stage		TNM Stage	
1	2	1	4
2	5	2	16
3	13	3	20

Table 1: Patient demographics to show stage and gender.

IMRT Planning Technique: Is previously described (8). Phase 1 (PH1) IMRT; prescription dose 30.6 Gy in 17 fractions followed by forward step-and-shoot PH2 plan of 19.8 Gy in 11 fractions. Table 2 shows the current constraints for the genitalia.

Genitalia Contouring: Original genitalia contours for the retrospective treated plan were defined by the clinical oncologist and their interpretation of the departmental protocol; males, penis and scrotum; females, the labia minora, majora and mons pubis. For study purposes the genitalia was re-contoured following the proposed genitalia contouring guidelines (7).

Data Collection and Statistical Analysis

The sample was divided into six sub-groups; females, males, female node negative (FNN), female node positive (FNP), male node negative (MNN) and male node positive (MNP). 'Node negative' and 'node positive' groups are defined as tumour stage with involved node(s). Dose volume histogram data, genitalia volume, PTV size and volume of genitalia overlapping with

PTV1 was compared. A statistical significance level of $P < 0.05$ is reported.

Results

- New genitalia contours were significantly larger than original contours ($p<0.00$). Difference (%) whole group 127.5%, F 126.1% and M 56.3%.
- V20Gy was 69.9% and 82.3% for all original and new genitalia contours respectively ($p=0.002$). V30 Gy was 38.7% and 43.7% for original and new genitalia contours ($p=0.003$).
- The majority of original and new genitalia contours failed to meet the current genitalia dose constraints.
- Female genitalia received significantly more radiation than male genitalia. This reached statistical significance for all parameters tested for new and original genitalia contours apart from original V50Gy.
- Patients with involved nodal disease received more genitalia irradiation than patients without involved nodal disease (Figure 2).
- Recommended genitalia dose constraints are displayed in Table 2. The dose constraints are rounded to the nearest whole number. The median DVH value of the sample denotes the optimal constraint and the 75th centile denotes the mandatory constraint.

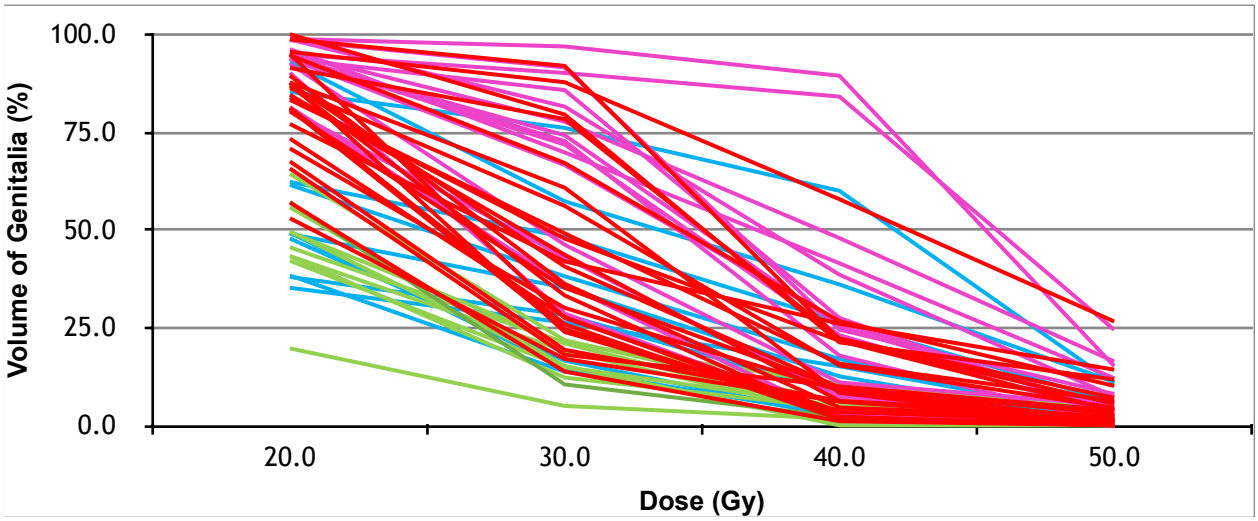

Figure 2: Genitalia doses for new genitalia contours. FNN=Red, FNP=Pink, MNN=Green and MNP=Blue.

Volume of Genitalia receiving X Gy (V_{XGy})			**V_{20Gy}**	**V_{30Gy}**	**V_{40Gy}**	**V_{50Gy}**
Current Constraints	All Patients		<50%	<35%	<5%	N/A
New Constraints	Female Node Negative	Optimal	<85%	<38%	<9%	<2%
		Mandatory	**<91%**	**<60%**	**<22%**	**<6%**
	Female Node Positive	Optimal	<94%	<72%	<25%	<4%
		Mandatory	**<96%**	**<85%**	**<41%**	**<11%**
	Male Node Negative	Optimal	<48%	<15%	<3%	<1%
		Mandatory	**<56%**	**<21%**	**<5%**	**<2%**
	Male Node Positive	Optimal	<49%	<32%	<14%	<1%
		Mandatory	**<68%**	**<50%**	**<29%**	**<7%**

Table 2: Current and suggested genitalia dose constraints.

Conclusion

The aim of this study was to quantify the genitalia dose differences between original genitalia contours defined by a clinician and new genitalia contours defined with the aid of a genitalia atlas. By following a genitalia contouring atlas it is expected that reproducibility and consistency of genitalia contours is improved between patients. This study concludes genitalia dosimetric differences exist between genders and patients with and

without involved nodes. The current generic set of genitalia dose constraints are inappropriate and dose constraints have been recommended that are gender and tumour stage specific. A limitation of these recommended dose constraints are that they are derived from a retrospective setting. There may be internal validity issues regarding the quality of the original IMRT plan due to the difficulty of meeting the original dose constraints. In addition one cannot say how well these new dose constraints will be met when applying to alternative techniques. These recommended dose constraints should be tested within a phase 1 clinical trial where genitalia acute and late toxicity can also be prospectively collected.

References

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