MAYO CLINIC

Intensity-modulated radiation therapy (IMRT) for anal cancer: results from a multi-institutional retrospective cohort study.

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BACKGROUND

Chemoradiation is the standard of care for anal cancer. Such a treatment has not been without toxicity [1] and some have suggested using IMRT to improve the tolerability of treatment [2-7]. The RTOG has treated patients on a multi-Institutional protocol using IMRT and has reported preliminary findings [4-5]. However, there has been some concern over the use of IMRT and a potential detriment to local control [8]. The current multi-institutional review was done to assess the outcomes in terms of disease control and toxicity for patients treated with IMRT for anal cancer.

METHODS

- A retrospective review of cases at each institution was combined for a total of 152 patients.
- Four were excluded for either presence of metastatic disease (2) or stage TX (2).
- Median prescribed radiation dose was 51.25 Gy (range, 4.32-61.2 Gy) in 28 fractions (2 - 34)
- Chemotherapy was given in all but two patients and the most common regimen was 5- fluorouracil (5FU) plus mitomycin-C (MMC).
- Endpoints evaluated included local control and survival
- Acute (< 6months from start of treatment) and late toxicity was scored at each institution

Table 2

	Acute Toxicity (Grade 3-5)
GI	17 (11%)
Heme	61 (41%)
Skin	30 (20%)
Other	1 (1%)
	Chronic Toxicity (Grade 3-5)
GI	3 (2%)
Skin	1 (1%)

RESULTS

Patient and Tumor Characteristics

- Table 1 shows the characteristics for patients in this study.
- The median follow-up was 26.8 months.
- The median elapsed days of radiotherapy was 40.

Overall Survival

- Overall survival at 3 years was 87%.

Local Control

- At a median follow-up of 26.8 months, the local control at 3 years was 87% and was significantly worse for patients with T3-4 disease compared with T1-2 (79% vs 90% at 3 years; p=0.04).

Regional/Distant Control

- Regional control for the entire groups at 3 years was 97%.
- Nodal stage predicted for nodal failure (P<0.01), but there was no significant relationship with radiation dose or type of chemotherapy.
- Similarly, distant control was 91% at 3 years and correlated with nodal stage (*P*<0.01).
- At 3 years, the distant control for patients with N0 disease was 97% (95% confidence interval, 89 - 99%), for N1 was 97% (95% confidence interval, 82 – 100%), for N2 was 87% (95% confidence interval, 59 – 97%), for N3 disease was 44% (95% confidence interval, 18 – 73%).

Need for Colostomy

- The estimated colostomy-free survival (CFS) was 92% at 3 years (95% confidence interval, 86 – 96%).
- Patients with T3-4 tumors had significantly worse 3 year CFS (84%; 95% confidence interval, 68 – 93%) compared to those with T1-2 disease (96%, 95% confidence interval, 90 – 98%, *P*=0.02).
- Even for the population with T4 tumors, the majority avoided colostomy at 3 years (74%, 95% confidence interval, 43 – 91%).

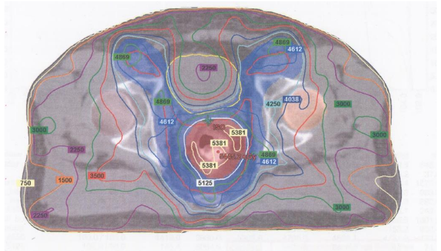
Toxicity (Table 2)

- The most common acute toxicity was hematologic , found in 41% of patients.
- Severe acute GI toxicity was 11% and severe acute skin toxicity was 20%.

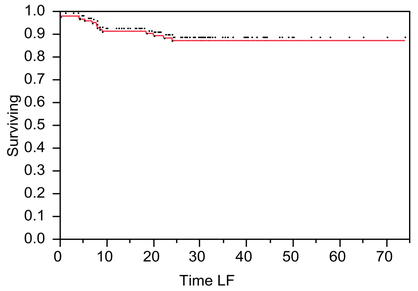
Table 1

Characteristic	Value
Age, median (range)	56 (32-86)
Dose, median	51.25 Gy
TNM Category	
T1	28
T2	79
T3	29
T4	12
N0	77
N1	40
N2	19
N3	12

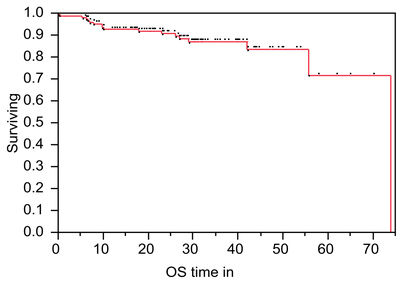
Figure 1. Example isodose distribution from a patient with a T2 N0 squamous cell carcinoma of the anus. The patient received 25 fractions of IMRT with a prescribed dose of 5125 cGy to the primary and 4250 cGy to elective nodal areas.



Local control. For all patients, the 3 year local control was 87%.



Overall survival. The 3 year Overall survival was 87%.



DISCUSSION

- Chemoradiation for anal cancer has been associated with high rates of severe toxicity [1]
- IMRT has been shown to decrease acute toxicity in a single arm prospective trial by the RTOG [5]
- Preliminary data from RTOG 0529 as well as small retrospective studies have indicate that IMRT for anal cancer is safe and effective [2-7]
- One institution has experienced suboptimal LC using IMRT a 3D conformal technique [8]
- This series adds to the literature of the effectiveness and tolerability of chemoradiation using IMRT.
- The most common acute severe toxicity with IMRT is hematologic
- The rate of non-hematologic toxicity with IMRT is encouraging

CONCLUSIONS

1. Chemoradiation utilizing IMRT resulted in a high rate of local control.
2. IMRT has an acceptable toxicity profile.
3. Higher nodal status is associate with worse disease outcome.

REFERENCES

1. Ajani, J.A., et al., *Fluorouracil, mitomycin, and radiotherapy vs fluorouracil, cisplatin, and radiotherapy for carcinoma of the anal canal - A randomized controlled trial.* Jama-Journal of the American Medical Association, 2008. 299(16): p. 1914-1921.
2. Salama, J.K., et al., *Concurrent chemotherapy and intensity-modulated radiation therapy for anal canal cancer patients: A multicenter experience.* Journal of Clinical Oncology, 2007. 25(29): p. 4581-4586.
3. Milano, M.T., et al., *Intensity-modulated radiation therapy (IMRT) in the treatment of anal cancer: Toxicity and clinical outcome.* International Journal of Radiation Oncology Biology Physics, 2005. 63(2): p. 354-361.
4. Kachnic, L., et al., *RTOG 0529: A Phase II Evaluation of Dose-painted IMRT in Combination with 5-Fluorouracil and Mitomycin-C for Reduction of Acute Morbidity in Carcinoma of the Anal Canal.* International Journal of Radiation Oncology Biology Physics, 2009. 75(3): p. S5-S5.
5. Kachnic, L., et al., *Early Efficacy Results of RTOG 0529: A Phase II Evaluation of Dose-painted IMRT in Combination with 5-Fluorouracil and Mitomycin-C for the Reduction of Acute Morbidity in Carcinoma of the Anal Canal.* International Journal of Radiation Oncology Biology Physics, 2010. 78(3, Supplement 1): p. S55-S55.
6. Pepek, J.M., et al., *Intensity-modulated radiation therapy for anal malignancies: a preliminary toxicity and disease outcomes analysis.* Int J Radiat Oncol Biol Phys, 2010. 78(5): p. 1413-9.
7. Kachnic, L.A., et al., *Dose-painted Intensity-modulated Radiation Therapy for Anal Cancer: A Multi-institutional Report of Acute Toxicity and Response to Therapy.* Int J Radiat Oncol Biol Phys, 2010.
8. Vuong, T., et al., *Changes in treatment toxicity pattern using the combined treatment of patients with anal canal cancer and early local recurrence results associated with the introduction of new radiation technologies: 3D conformal therapy and intensity modulated radiation therapy.* J Clin Oncol (Meeting Abstracts), 2008. 26(15_suppl): p. 4608-.