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**TITLE**

**Aggressive Fibromatosis Treated with Radiotherapy: A Single Institution Experience with Adult Patients**

**HYPOTHESIS:**

This is not a hypothesis driven study.

**BACKGROUND/AIMS:**

Aggressive fibromatosis (desmoid tumor) is subject to varied and sometimes controversial management. The purpose of this study is to report the long-term disease control and toxicity outcomes in a large case series of patients treated with radiotherapy for this rare tumor.

**METHODS:**

We retrospectively analyzed 69 consecutive adult patients treated with radiotherapy at a single institution over a 40-year period (1975 to 2015). The median age was 41 years old (range, 31 – 80). Sixty-seven percent of patients were female; 65% were white. Fifty-five percent of patients were treated with radiation therapy at initial presentation for unresectable disease, primarily due to close anatomic proximity to vital structures. A minority of patients (16%) had 3 or more surgeries before radiotherapy. Further, 75% of patients had gross disease present at the time of radiation. Data on tumor size was available for 57 patients; the median maximum linear dimension was 8 cm (range, 2 – 22 cm). The median total radiotherapy dose was 54 Gy (range, 35 Gy – 70 Gy). Twice-daily fractionation (typically 1.2 Gy per fraction) was used in 36% of patients. Median follow-up was 14.2 years (range, 0.3 – 41.5 years). Cox proportional hazards modeling was used to compare the risk of local recurrence between various demographic, tumor, and treatment characteristics. Age and radiation dose were evaluated using a dichotomous model.

**RESULTS & CONCLUSIONS**

Overall survival rates at 5, 10, and 15 years were 98.2%, 92.6%, and 83.0%. The local control rates at 5, 10, and 15 years were 88.9%, 87.0%, and 87.0%, respectively. On univariate analysis, age <40 years was associated with inferior local control (5-year local-regional control rate, 78% versus 97%; hazard ratio = 4.4; 95% confidence interval = 1.0 – 30.0;  $p = 0.048$ ), a trend which was maintained on multivariate analysis ( $p = 0.048$ ). Neither the presence of gross disease nor recurrent disease was associated with an increased risk of recurrence. There was no statistically significant difference in local control between patients who received <55 Gy and those who received  $\geq 55$  Gy ( $p = 0.70$ ). A total of 39% of patients developed grade 3 or higher acute or late treatment-related toxicity; the most common toxicity was lymphedema, occurring in 13% of patients. The second most common toxicity was pain/paresthesia, occurring in 12% of patients. There were 2 in-field fractures identified. Treatment toxicities were more frequent in patients who received surgery before RT (47%) relative to those who did not (32%), although this finding was not statistically significant ( $p = 0.32$ ).

Moderate-dose radiation is associated with high rates of local control and acceptable toxicity. Radiotherapy should be considered the standard of care for adult patients with recurrent or unresectable aggressive fibromatosis.