Radiation therapy for breast cancer in patients with Li-Fraumeni syndrome (LFS): a single institution cohort study

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Background

Li-Fraumeni syndrome (LFS) [1], caused by monoallelic germline pathogenic variant (PV) in **TP53 gene**, causes an elevated risk of developing certain cancers, mainly early onset breast cancer, sarcoma and brain tumors **[2]**.

While LFS patients are believed to be at an increased risk for **radiation-induced sarcomas (RIS)**, only a few retrospective studies **[3]** have been published studying the impact of radiation therapy in the treatment of breast cancer among these patients.

This study reviews the data concerning LFS patients treated at the **Institut Curie** with adjuvant radiation therapy for localized breast cancer.

Methods

Retrospective study conducted on LFS female breast cancer patients treated at the Institut Curie.

Inclusion criteria :

- Confirmed TP53 PV
- Non metastatic disease at diagnosis
- Histologically confirmed breast malignancy
- Data available concerning administration of radiotherapy during the initial treatment regimen

Patient characteristics, tumor features, treatment details, and outcomes were extracted from electronic medical records.

Continuous variables were described as median with interquartile range (IQR) or mean with standard deviation. Categorical variables were expressed as frequencies and percentages. Survival analyses were performed using Kaplan-Meier methods, and curves were compared using log-rank tests. Univariate Cox proportional hazards regression models were used to evaluate the impact of radiotherapy and other clinical variables on survival outcomes.

Results

From 1989 to 2025, we identified **39 female LFS breast cancer** patients who met our inclusion criteria. Median follow-up was **95 months** (IQR: 26-157).

61.5% of patients had a family history suggestive of LFS.

Characteristics	number (n=39)	%
Age, y, median (range)	29 [24-44]	
BMI, median (range)	22 [15-38]	
Histological type		
DCIS	6	15.38%
IDC	26	66.67%
ILC	1	2.56%
other	5	12.82%
NA	1	2.56%
cT		
Tis	6	15.38%
T1	8	20.51%
T2	14	35.90%
T3	3	7.69%
T4	3	7.69%
TX	5	12.82%
cN		
N0	25	64.10%
N1	6	15.38%
N2	3	7.69%
N3	2	5.13%
NX	3	7.69%
Receptor status		
HR+/HER2-	10	25.64%
HR+/HER2+	8	20.51%
HR-/HER2+	7	17.95%
TNBC	2	5.13%
NA	12	30.77%
Grade		
Intermediate grade DCIS	4	10.26%
High grade DCIS	2	5.13%
grade I (invasive)	1	2.56%
grade II (invasive)	14	35.90%
grade III (invasive)	15	38.46%
NA	3	7.69%

Table 1. Patient Characteristics

Overall survival (OS) at 5 and 10 years was 82.5% (95% CI: 70.7-96.3%) and 64.0% (95% CI: 48.8-84.0%) respectively.

Surgery type, chemotherapy administration, T stage (Tis-T1-T2 vs T3-T4), N stage (N0 vs N+), and receptor status (TNBC vs HER2+ vs HR+/HER2-) showed no significant association with overall survival in univariate analyses.

21 patients received radiotherapy as part of their initial treatment regimen. Patients treated with radiotherapy had a higher proportion of clinically node positive disease (43% vs 11%) and T3-T4 tumors (24% vs 5.6%) at initial staging.

No RIS case satisfying the Cahan criteria [4] was found within this cohort, yet four patients later developed new malignancies arising within the previously irradiated fields for breast cancer.

Radiotherapy showed no significant impact on cancer-specific survival, nor locoregional recurrence-free survival (all p>0.05).

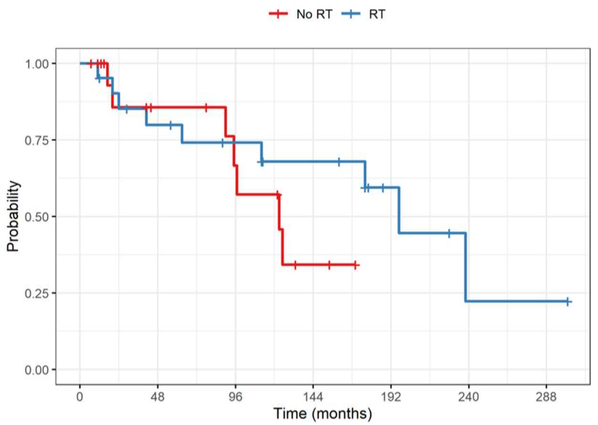


Figure 1. Overall Survival (p=0.28)

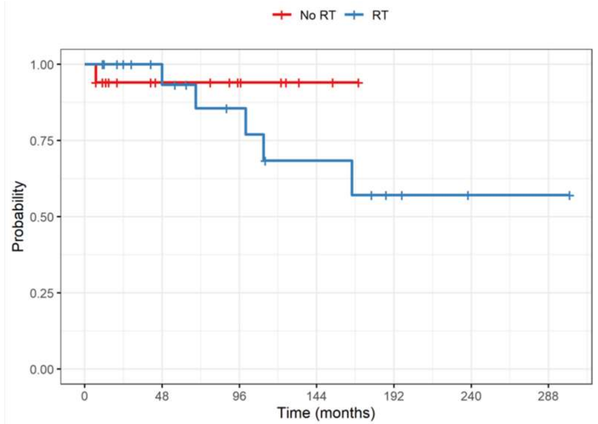


Figure 2. Locoregional Recurrence-Free Survival (p=0.34)

Discussion

This study did not identify any RIS despite a long median follow-up, possible explained by factors such as retrospective study limitations, latency periods exceeding 10 years, and the potential inadequacy of Cahan criteria to detect non-sarcomatous secondary cancers in LFS.

Despite inherent limitations, the cohort's size and follow-up strengthen its relevance, **providing cautious reassurance when radiotherapy is clinically indicated in LFS patients.**

Conclusions

The incidence of RIS in LFS breast cancer patients was lower than anticipated. Further studies with larger cohorts and extended follow-up are required to validate these findings.

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