

# Levels of Circulating Tumor DNA (ctDNA) Correlate with Disease Status in Patients with Soft Tissue Sarcomas: A Pilot Study

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## INTRODUCTION:

Circulating tumor DNA (ctDNA), tumor-derived DNA fragments found in the bloodstream, has shown potential for monitoring minimal residual disease (MRD), treatment response, and recurrence in select solid tumors including lung, colorectal, and breast cancers. However, its clinical utility in soft tissue sarcomas remains unknown. This pilot study aims to evaluate the feasibility of ctDNA detection in soft tissue sarcomas and its correlation with disease status based on radiologic surveillance.

## METHODS:

At a single institution, two orthopaedic oncologists used a personalized assay to quantify ctDNA in patients with biopsy proven soft tissue sarcomas at presentation (baseline) and multiple follow-up intervals (2022-2025). All patients received standard of care treatment and surveillance via magnetic resonance imaging (MRI) of the affected limb and chest computed tomography (CT). The orthopaedic oncologists were not blinded to the ctDNA results however, the results did not alter treatment or surveillance decisions. Patients  $\geq 18$  years with a baseline ctDNA were included in this retrospective cohort study.

## RESULTS:

A total of 12 patients were included in this pilot study, with a mean age of  $56.1 \pm 16.2$  years. The mean tumor diameter was  $11.8 \pm 5.8$  centimeters (cm), and the mean follow-up after resection was 13.8 months ( $n = 5$ ). Baseline ctDNA was detectable ( $>0$ ) in 10 patients (83.3%). Two patients with undetectable ctDNA had low- or intermediate-grade sarcomas. The highest ctDNA was observed in a patient with a large tumor and metastatic disease at presentation. Baseline ctDNA levels showed a statistically significant strong positive correlation with tumor diameter on MRI (Spearman's correlation,  $r = 0.76$ ,  $p = 0.0018$ ). Postoperative ctDNA decreased to zero in all patients who underwent resection. Patients who maintained follow-up ctDNA of zero had no radiologic evidence of disease.

## DISCUSSION AND CONCLUSION:

This pilot study demonstrates the feasibility of using a personalized assay to detect ctDNA in various soft tissue sarcomas. Higher baseline ctDNA correlated with larger tumor size, an indicator of disease burden, suggesting potential prognostic and surveillance utility. The small sample size is a limitation of this study, underscoring the need for larger prospective studies to further evaluate the clinical value of ctDNA in this population.

Table 1 Patient pathology, ctDNA, and radiologic information

Patient	Pathology	Baseline ctDNA	Largest Diameter MRI (cm)	Baseline CT Chest	Most Recent ctDNA	Most Recent Imaging Results	Patient Status
1	High grade myxoid liposarcoma	7.41	14.8	NED	N/A	N/A	Lost to follow-up
2	High grade myxofibrosarcoma	254.77	16.4	NED	0	NED	NED
3	High grade UPS	15.29	19.1	NED	0	NED	NED
4	High grade UPS	85.92	11.2	NED	N/A	N/A	Deceased
5	Intermediate grade myxofibrosarcoma	0	4	Benign nodules	0	NED	NED
6	High grade small round cell sarcoma	3317.32	19.5	Metastases	N/A	N/A	Deceased
7	High grade pleomorphic rhabdomyosarcoma	4.08	4.4	NED	N/A	N/A	Post resection, awaiting follow-up
8	Low grade fibromyxoid sarcoma	0	7.7	Benign nodules	0	NED	NED
9	Low grade extraskeletal myxoid chondrosarcoma	0.92	14.3	Benign nodules	0	NED	NED
10	High grade pleomorphic spindle and epithelioid cell sarcoma	0.43	9.8	NED	N/A	N/A	Post resection, awaiting follow-up
11	Intermediate grade leiomyosarcoma	1.57	4	Benign nodules	N/A	N/A	Awaiting follow-up
12	High grade pleomorphic rhabdomyosarcoma	484.55	16	Benign nodules	N/A	N/A	Post resection, awaiting follow-up

cm, centimeters; N/A, not applicable; NED, no evidence of disease; UPS, undifferentiated pleomorphic sarcoma