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Nano mechanical Investigation of Extracorporeal Irradiation and Re-implantation Therapy in Malignant Bone Tumors

S Chauhan[1]; Dr K Manoj[2], MBBS; Prof. S Rastogi[2] MD; Dr SA Khan[2],MD; Dr A Prasad[1], PhD,Dr.D.N.Sharma*

*[1]Applied Mechanics, Indian Institute of Technology, Delhi, India (*aprasad@am.iitd.ac.in)*
[2]Orthopedics, All India Institute of Medical Sciences, New Delhi, India

Introduction: Extracorporeal irradiation therapy (ECRT) and reimplantation is now an established technique for limb salvage surgery of malignant bone tumour. ECRT is a biological reconstruction method with several advantages including no risk of immunological reaction or diseases transmission, cost-effective, absence of heavy implants, no need for subsequent surgeries in growing-age patients, and others. While several studies have focused on clinical outcome of the procedure, structural and changes in human bone under heavy dose of radiation (50 Gy) are not well established. Here we examine biomechanical property in resected bone for patients with malignant bone tumors (osteosarcomas and Ewing's sarcoma) pre and post ECRT.

Materials and Methods: We have so far examined 5 patients with MBT undergoing ECRT at All India Institute for Medical Sciences (AIIMS), and subsequent biomechanical study being performed at Indian Institute of Technology Delhi (IIT-Delhi). There were four males and one female patient, with mean age of 18 years. The femur, pelvis, and tibia are the concern locations. From the resected bone sample of excised tumor bone was obtained pre and post ECRT and delivered in physiologically saline solution to IIT Delhi. The excised samples were cleared of bone marrow (defatting) and excess of soft tissue using jet of deionized water and kept in desiccators for an hour. The sample is embedded in epoxy and subsequently polished for mechanical testing. The indentation is carried out on pre and post irradiated embedded bone sample (Universal Nanomechanical Tester, ASMEC, Germany). Nanoindentation with quasi-continuous stiffness measurement mode is carried out using geometrical self-similar Berkovich diamond tip with radius of 184 nm with maximum load of 25 mN and indent spacing of 50μm. To quantify the contact area of the indent and to study regarding viscoelastic or time–dependent property of the specimen, atomic force microscope (Nanosurf Nanite B Liestal, Switzerland) is used. This study also aims to investigate the compositional changes occurring due to irradiation through detailed study of Raman spectroscopy using 785nm.

Results and Discussion: Average indentation curve obtained by series of indentation at the location of secondary osteon revealed loss of strength via reduced modulus for all the five specimens. Through AFM study it is evident that indentation on post radiation sample shows significant amount of pile up which indicates softening effect of irradiation. Raman spectroscopy analysis reveals reduction of mineral content in the post-irradiated bone, thus making the bone softer in nature. Thus these set of data reveal that bone undergoes significant compositional and mechanical property changes as a result of high-dose radiation. Additional tests on samples as well as for new patient cases (total cases planned are 15) are currently ongoing to further establish the results.

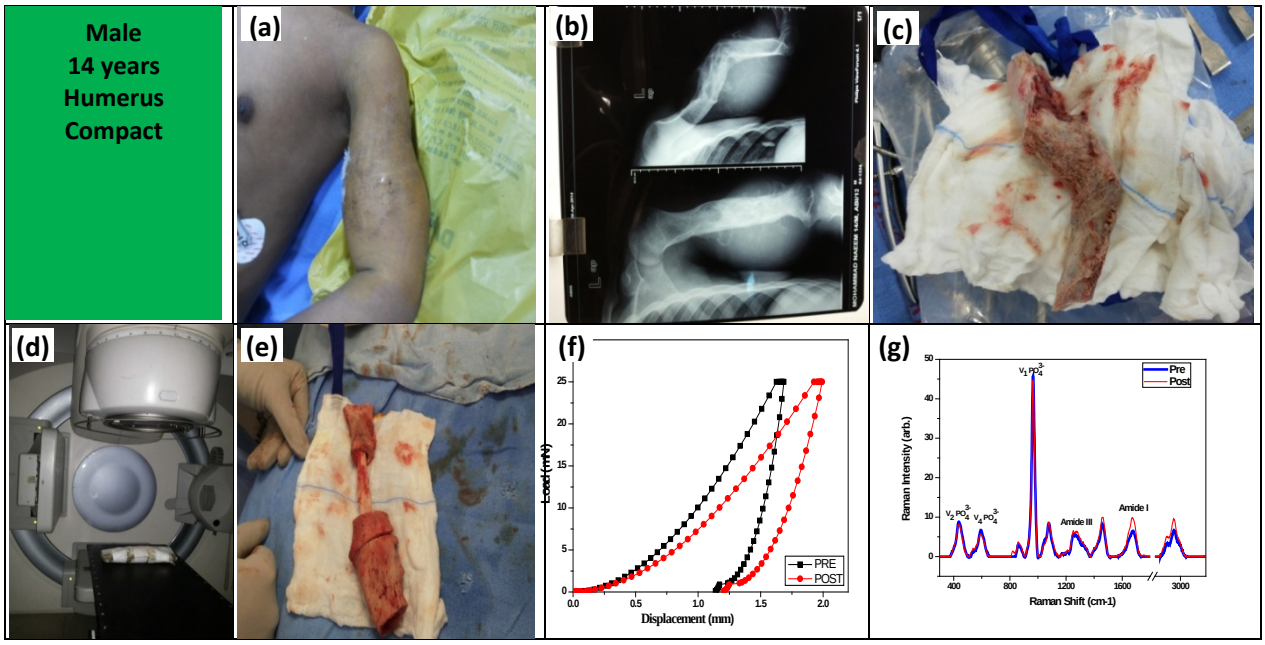

Figure 1 (a) 14 years male humerus section suffering from Ewing sarcoma; (b) Patient CT scan; (c) Resected Bone pre-radiation; (d) bone undergoing 50Gy radiation in isolated chamber ;(e) cleaned and treated bone post radiation; and (f) Typical indentation curve of normal sample obtained for pre and post-radiation bone sample (g) Raman Spectrum

Conclusions: We have characterized structural and mechanical property changes for patients under ECRT. Such data can help clinicians in selection of suitable external support mechanism (such as locking plates, intramedullary nails, simple K wires, or pins) during reimplantation, and in deciding post-operative care.