STUDY OF REGRESSION OF BREAST TUMOR IN MICE MODEL USING MRI

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Introduction: Breast cancer remains the major cancer among women, which is associated with high mortality and morbidity. Epidemiological studies indicate that the incidence of the breast cancer is influenced by familial, endocrine and dietary factors. Molecular iodine (I_2) has been shown to cause apoptotic cell death independent of estrogen receptor and p53 status in breast cancer cell lines (MCF-7, MDA-MB-231, MDA-MB-453, ZR-75-1, T-47D). Antimalarial agent such as Chloroquine reduces proliferation in cellular models, but impairs spontaneous lymphoma development in a mouse mode. It also evidenced that a short prior exposure to chloroquine is preventative against N-methyl-N-nitrosourea (NMU-induced mammary carcinogenesis [1,2]. In this direction, we have undertaken MRI studies to measure the periodical growth of tumor in control, I_2 treated and Chloroquine with I_2 treated mice model.

Materials and Methods: A total of 20 ICRC mice were used. Tumor pieces of 3-4mm^3 from a spontaneous mammary tumor (MDA-MB-231) were subcutaneously transplanted. After 2 weeks of tumor transplantation mice were randomly divided into 3 groups Control (n=5), Treatment 1(Tr1, n=7) orally received I_2 (0.5mg/kg bodyweight/day) and Treatment 2 (Tr2, n= 8) administered with chloroquine intramuscularly 40mg/kg/day along with I_2 (orally) for 6 weeks and tumor volume was measured at different time points. For MRI the mice were anesthetized by intraperitoneal injection of ketamine (200 mg/kg body weight) and Xylazine (16 mg/kg body weight). All the measurements were carried out at 9.4 T using Bruker Biospin NMR wide bore (80 mm) spectrometer with micro-imaging accessories. T_1-weighted 2D MRI images were obtaining using spin echo (SE) pulse sequence with TR/TE = 500/13 ms, slice thickness = 1mm, interslice thickness 1mm, field of view (FOV) = 35×35 mm^2, matrix = 256 × 256, 4 averages. The growth of tumor was monitored through MRI after 2 weeks of grafting. The tumor size measured at 2 weeks was considered as a positive control and the measurements were done at every 2 weeks until 8 weeks from the day of grafting. The tumor size was assessed in each serial MR images by Region Of Interest (ROI) based measurements [3]. Differences between categorical variables were analyzed using Mann–Whitney U-test, significance ($p \geq 0.05$). The tumor regression rate was determined as the percentage residual tumor volume by dividing the tumor volume at a given time point (i.e. at 4, 6, 8 weeks) by the initial tumor volume (two weeks).

Results: The axial T_1–weighted images of mice showing the MR image with the largest tumor cross-section is shown in fig 1. The tumor region was shown in the polygon. From the figure it is clearly clear that the systematic increase in the tumor size in control group. Whereas, significant decrease in the tumor size in Tr2 group was observed (Fig 1), initially and thus effectively reducing the tumor size when compared with Tr1 at eighth week (fig 2).
The percentage residual tumor volume, for I_2 treated group (Tr1) *Vs* Control. is 13, 43, and 60%, whereas combined I_2 with Chloroquine (Tr2) Vs Control. is 94, 76, and 60% in 4th, 6th and 8th week of tumor implantation respectively.

Discussion: The tumor volume measurement indicates that tumor volume in untreated mice showed a significant increase over a period of 6 weeks, Significant decrease in tumor size of Tr2 group when compared with Tr1. these results indicates that the chloroquine probably increases the therapeutic efficacy of the drug molecular iodine.

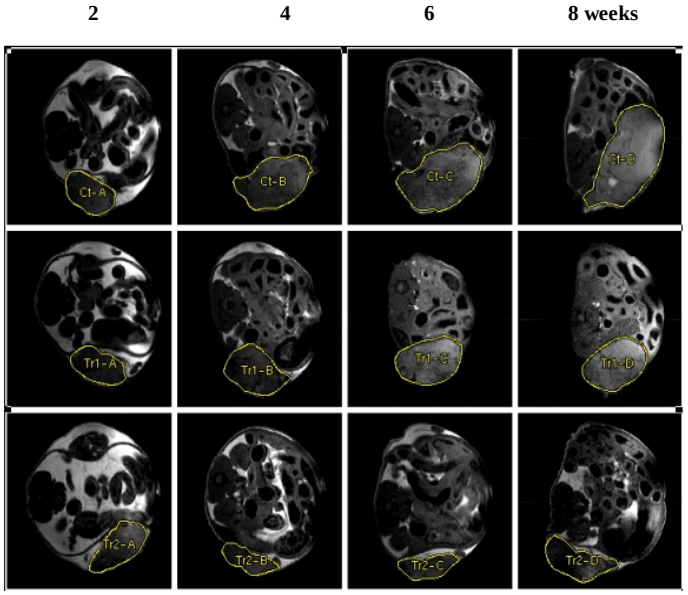

Fig 1: MR images of Control, Tr1 and Tr2 of the tumor grafted mice images at 2, 4, 6 and 8 weeks from the day of grafting

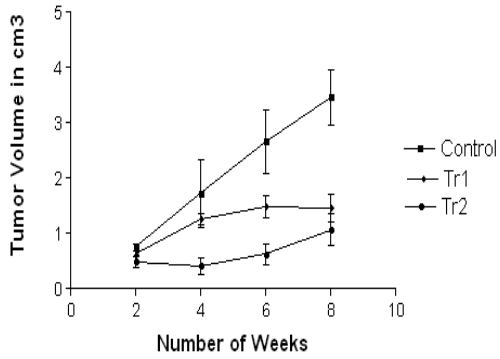

Fig 2: Plot of growth of tumor size *Vs* weeks.

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