

differences among the patients that could be explained by individual radiosensitivity.

**Materials and Methods:** The salivary gland ejection (excretion) fraction (sEF) was measured by Tc-99m pertechnetate scintigraphy for 50 patients receiving IMRT for head and neck cancer. The scintigraphy was performed before RT and repeated 6 and 12 months after RT. Only the glands with  $D_{\text{mean}}$  values between 15 Gy and 45 Gy were included and the glands which were not functioning properly prior to RT were excluded. The relative ejection fraction  $rEF(t) = sEF(t) / sEF(0)$  was first compared for both parotid glands of the same patient at the same time of measurement. Next, the rEF values at 6 and 12 months after RT were compared for the same gland. To enable the comparison of rEF values between glands receiving varying  $D_{\text{mean}}$ , the mean effect of the absorbed dose on the gland was eliminated. This was achieved by dividing the rEF value for the gland with the respective value of sigmoidal mean dose response curve for the whole group of patients ( $rEF_0 = rEF(t) * (1 + (D_{\text{mean}}/D_{50})^k)$ ). Fisher's exact test was used in the analysis with two categories defined by median  $rEF_0$ . Average errors in  $D_{\text{mean}}$  values for the glands due to patient positioning errors were corrected based on portal images.

**Results:** The values for  $rEF_0$  ranged from 0 to 2.7. A significant association between  $rEF_0$  for left and right parotid glands was found ( $\chi^2=6.0$ ,  $p<0.025$ ). Some patients show systematically lower or higher  $rEF_0$  than the median for both parotid glands. This could be explained by three possible reasons, as the effect of positioning errors to  $D_{\text{mean}}$  was excluded: 1) the variations result from the measurement technique or 2) the patients react differently to the lemon juice stimulus given during the scintigraphy or 3) the post-RT sEF is affected by varying individual responses to radiation. The  $rEF_0$  values for the same gland at 6 and 12 months after RT gave a statistically significant relationship between the two variables ( $\chi^2=4.73$ ,  $p<0.05$ ) (Table 1). The same patients had low or high values of  $rEF_0$  for both parotid glands at both times of measurement. As this behaviour is seen in both measurements, it can not be due to fluctuations caused by measurement technique. Also, we believe that by using relative values instead of single sEF values, we can at least partly overcome the problem of patients reacting differently to the stimulus, assuming that the factors, such as smoking, that may influence saliva production remain the same between the measurements. As a result of this indirect deduction, we conclude that the systematic variation in  $rEF_0$  reflects individual differences in radiosensitivity.

	$rEF_0$ (6 months) below median	$rEF_0$ (6 months) above/equal to median	Total
$rEF_0$ (12 months) below median	18	10	28
$rEF_0$ (12 months) above/equal to median	12	21	33
Total	30	31	61

**Conclusions:** According to our interpretation the systematic variations seen in post-RT salivary gland scintigraphy measurements can be explained by individual differences in radiosensitivity. Quantitative extraction of individual radiosensitivity requires further studies.

#### PO-0907

##### Magnetic ferrofluid hyperthermia for breast cancer treatment

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**Purpose/Objective:** Ferrofluid particles being subjected to an electromagnetic field show remarkable heating effects related to losses during the magnetization process and Joule heating of the particles. The temperature enhancement which occurs in a magnetic ferrofluid system under the influence of an external high frequency magnetic field has found applications in breast tumor hyperthermia treatment therapy. The main objectives are the uniformity of the temperature distribution and the target value of temperature to be up

to 42°C in the controlled region for magnetic hyperthermia treatment. This temperature control is hard to implement because of many tissue individual variations and other therapy conditions.

**Materials and Methods:** For determination of the thermal field distribution in magnetic hyperthermia therapy, a coupled electromagnetic - thermal - fluid dynamics field computational model is developed. The electromagnetic field distribution inside the conductive tissue region depends on the time varying magnetic flux density. The heat sources are defined by the electric losses in tissue, acquired by the solution of the electromagnetic field problem. The computational model uses anatomically precise multilevel geometrical model of human breast with known electrical tissue properties, blood and liquor flow speeds in its vessels. Model contains information about real cancer structure sample acquired by surgical procedure. Cancer and normal electrical tissue properties are directly measured for this sample by precise measurement system.

**Results:** Sample under treatment is in stage T2N2M1 with maximal size of 25 mm. Sample volume is 317 mm<sup>3</sup>. Ferrofluid solution is injected at cancer sample. Ferrofluid filled volume in sample is 24 mm<sup>3</sup>. Thermal field distribution in cancer model is presented in Fig.1. Maximal temperature acquired is 42.3°C. Temperature maximum represents the position of ferrofluid volume. Results from this model are validated by infrared thermography measurements of the sample. Field values and distributions correspond well to these one acquired by the model.

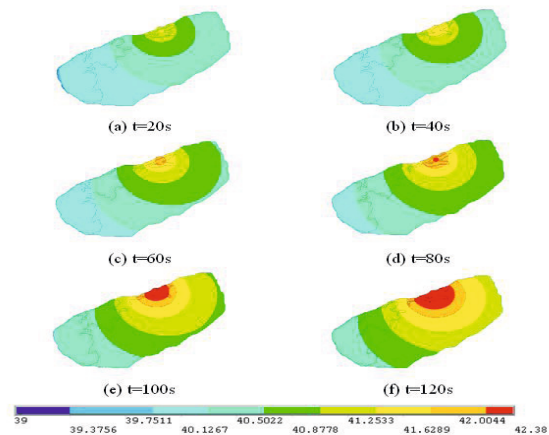


Fig.1 Thermal field distribution in tumor model for time period of 120s.

**Conclusions:** The coupled electromagnetic-fluid dynamics-thermal field computational modeling is capable to predict the magnetic ferrofluid hyperthermia thermal effects on live tissue. The developed model can be used for therapy planning and also design and optimization of interaction between electromagnetic devices and biological structures.

**Acknowledgement:** This work was supported by the National Science Fund of the Ministry of Education and Science of Bulgaria under Contract D002-157/2008'.

#### PO-0908

##### Identification of a single nucleotide polymorphism associated with sexual dysfunction in prostate cancer patients

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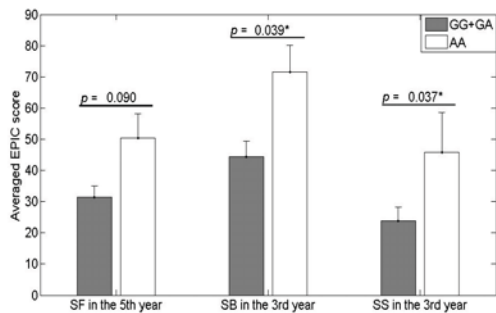
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**Purpose/Objective:** To study whether genetic single nucleotide polymorphisms (SNPs) are predictive of erectile dysfunction (ED) in prostate cancer patients treated with radiotherapy, we investigated the relationship between genotypes in SNP data and Expanded Prostate Cancer Index Composite (EPIC) scores.

**Materials and Methods:** In our previous study, we examined SNPs obtained for 124 prostate cancer patients who received radiotherapy (RT) and, after identifying a statistically-managable number of SNPs using a novel system biology approach, we identified a single SNP (rs2032809) that was statistically associated with post-RT adverse

genitourinary (GU) and/or gastrointestinal (GI) late toxicity with  $p = 0.0043$  after Bonferroni correction in a recessive SNP model. This SNP belongs to BBC3/PUMA that plays a critical role in DNA damage-induced apoptosis. EPIC-validated quality-of-life questionnaires were surveyed for these patients with a maximum follow-up of 5 years. In this study, we further tested the relationship between rs2032809 and EPIC scores (sexual function [SF], sexual bother [SB], and sexual domain summary [SS]).

**Results:** At baseline, the mean SF, SB, and SS scores were 44.63 (95% confidence level [CI]: 39.53 - 49.45), 63.52 (95% CI: 58.20 - 69.13), and 50.40 (95% CI: 45.43 - 55.03), respectively. At 5-year follow-up, the mean SF, SB, and SS scores decreased by 41%, 30%, and 40%, respectively. A Mann-Whitney U test was used to investigate relationship between rs2032809 and EPIC scores. Significant associations were found with third-year SB ( $p = 0.039$ ) and SS ( $p = 0.037$ ) scores (Figure 1). In the third year, the mean SB scores for those who have and do not have the minor allele were 71.53 and 44.49, and 50.33 and 31.47 for the mean SS score, respectively, suggesting a considerable protective effect of this SNP. An additional test between the SNP and a fifth-year SF score yielded a borderline significant estimate ( $p = 0.090$ ) and the mean SF scores were 45.76 and 23.85, respectively, for those who have and do not have the minor allele.



**Figure 1.** Comparison of mean EPIC scores (+standard error of the mean) for patients who have GG+GA and AA genotypes in rs2032809 using Mann-Whitney U test. SF: sexual function; SB: sexual bother; SS: sexual domain summary.

**Conclusions:** We further examined a single BBC3/PUMA gene SNP (rs2032809) that was identified as a candidate biomarker of GI/GU toxicity in prostate cancer patients with a hypothesis as to whether this SNP is also correlated with sexual dysfunction. We observed a statistically significant association between the SNP and the third or fifth-year ED of patients. This further strengthens the evidence that this apoptosis gene is an important determinant of late toxicity and is affected by rs2032809.

## POSTER: PREVENT TRACK: EFFECTS OF BIOLOGICAL MODIFIERS ON NORMAL TISSUE TOLERANCE (AMELIORATION / EXACERBATION)

PO-0909

Comparison of protective effect of melatonin and amifostine on acute renal damage caused by ionizing radiation

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**Purpose/Objective:** The aim of this study is to compare the protective effect of melatonin and amifostine on radiation induced acute renal damage.

**Materials and Methods:** Fifty female albino rats were divided into five groups (with ten rats each): control (Cont), radiotherapy alone (RT), radiotherapy + amifostine (RT+AMI), radiotherapy + melatonin (RT+MEL), radiotherapy + amifostine + melatonin (RT+AMI+MEL). All experiments were conducted adhering to the guidelines of the institutional animal ethics committee. RT group were treated with only 0.9% saline solution 30 min before irradiation. Intraperitoneal amifostine (200 mg/kg) was administered to the rats in the RT+AMI and RT+AMI+MEL groups 30min before irradiation. Intraperitoneal

melatonin (100 mg/kg) was administered to the rats in the RT+MEL and RT+AMI+MEL groups 30 min before irradiation. RT, RT+AMI, RT+MEL and RT+AMI+MEL groups were irradiated individually with a single dose of 8 Gy on whole body, using a Co-60 treatment unit (Cirrus,cis-Biolnt., Gif-sur-Yvette,France). Dose rate was 1.15 Gy/min. At the end of the follow-up period (72 hours) sacrifice was done in all groups. Paraffin embedded kidney tissue samples were analyzed and percentage of damaged glomeruli was determined by counting damaged glomeruli of kidney cortex as segmental or total necrosis for each animal.

**Results:** The percentage of damaged glomeruli is presented in Table 1. The protective effect of amifostine, melatonin, and amifostin plus melatonin on radiation induced renal toxicity is statistically meaningful ( $p = 0.000, 0.003, 0.000$ , respectively). There is an advantage in favor of melatonin when compared with amifostine ( $p = 0.005$ ). Although there is not an advantage of adding amifostine to melatonin when compared with melatonin alone ( $p = 0.243$ ), there is statistically significant better protective effect in amifostine plus melatonin group when compared with amifostine alone group ( $p = 0.003$ ). As there was no significant damage following 8 Gy whole body irradiation on the kidney tubule, the protective effect of any agent could not be assessed.

**Table 1.** The percentage of damaged glomeruli

Groups	Cont	RT	RT+AMI	RT+MEL	RT+AMI+MEL
Glomeruli damage (%)	0	40	30	20	20
	0	40	40	20	30
	0	50	40	30	30
	0	40	30	25	30
	0	50	20	20	20
	0	40	30	20	15
	0	40	30	25	20
	0	50	40	30	15
	0	40	40	20	15
	0	40	30	30	20

**Conclusions:** In this study, it has shown that the protective effect of melatonin on radiation induced acute renal toxicity is better than amifostine. These results are encouraging for the clinical use of melatonin.

## POSTER: PREVENT TRACK: RADIATION EFFECTS ON SPECIFIC ORGANS / TISSUE

PO-0910

Dose to the anal-sphincter region and the rectum and faecal leakage after radiation therapy for prostate cancer.

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**Purpose/Objective:** To investigate possible synergetic effects between dose to the anal-sphincter region and dose to the rectum for the occurrence of long-term fecal leakage after radiation therapy for prostate cancer.

**Materials and Methods:** For the current analyses we included 414 prostate-cancer survivors who had received external beam radiation therapy (EBRT) to a total dose of 70 Gy in 2 Gy daily fractions between 1993 and 2006. We also included 332 population-based controls matched for age and residency. EBRT was delivered using one anterior-posterior and two lateral wedged field. The planning target volume comprised the prostate or post-operative prostatic region with 20 mm margin except for the rectal margin, which was 15 mm or maximum half the rectal cross-sectional area. We restored original