WIDEST-WIDESpread Tumors BNCT

CONSUNTIVI 2011

S.ALTIERI, S.BORTOLUSSI, F.BALLARINI, S.STELLA, N.PROTTI, A.DE BARI, R.NANO

Participants

	Nome	Qualifica	Aff.	%
1	Altieri Saverio	Ricercatore	CSN V	50
2	Ballarini Francesca	Ricercatore	CSN V	40
3	Bortolussi Silva	Ricercatore TD	CSN V	40
4	De Bari Antonio	Ricercatore	CSN V	20
5	Nano Rosanna	Prof. Ordinario	CSN V	100
7	Nicoletta Protti	Dottoranda-Assegnista	CSN V	100
8	Sabrina Stella	Dottoranda	CSN V	100
				4.5

Activities extention

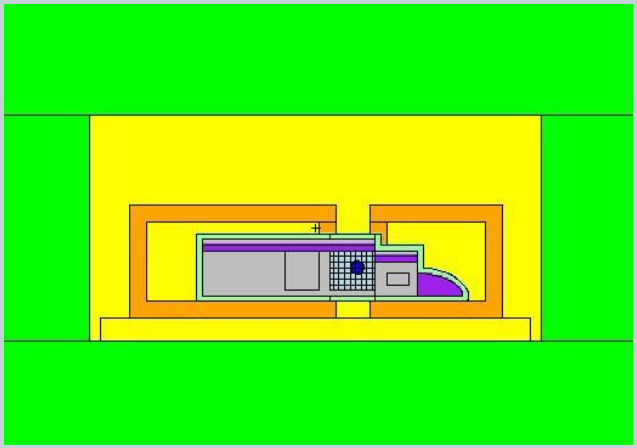
- 1. Rat Irradiation…Last year: *unfortunately, bureaucracy difficulties related to the setting of the biologic laboratory were the animals should be kept, are seriously delaying this part of the investigation planned*

- 2. Measurements of boron uptake in patients…Last year new collaborations were started with HUCH (Helsinki), IOV (Padova) and Hospital of Catanzaro.

1. Rats irradiation

- The bureaucracy was completed and we got the permission to irradiate the animals and keep them at the laboratory of Botta 2. The shield made up of 95% Li-6 Carbonate was completed and used for the experiments. The shielding material was obtained thanks to the collaboration with INL (Idaho National Laboratory), in particular with Dr.Ing. David Nigg.
- In order to irradiate rats: deep study of the dosimetry by MC calcs and esperimental neutron flux measurement by neutron activation of foils. Test of efficacy of the shield.

Shield and set-up



INL
Idaho National Laboratory

	ID ratto	Tipologia animale	tempo irr	data irr	Data morte	Giorni oss post irr	giorni oss dall'inoculo
1	R8			25/01/2012	26/01/2012	prova	-
2	R9			25/01/2012	25/01/2012	prova	-
3	R10			25/01/2012	05/03/2012	+39	-
4	R19			31/01/2012	30/03/2012	+59	-
5	R20			31/01/2012	30/03/2012	+59	-
6	R3	K B+		21/02/2012	16/03/2012	+24	+51
7	R4	K B+		21/02/2012	29/02/2012	+8	+36
8	R15	K B-		22/02/2012	05/04/2012	+6	+39
9	R16	K B-		22/02/2012	06/03/2012	+8	+40
10	R11	K B+		28/02/2012	03/04/2012	+4	+37
11	R17	K B-		28/02/2012	12/03/2012	+13	+46
12	R13	K B+		29/02/2012	15/03/2012	+15	+48
13	R14	K B+		29/02/2012	12/03/2012	+12	+46
14	R24	K B+		6/03/2012	5/04/2012	+30	+57
15	R25	K B+		6/03/2012	vivo		

16	R32	K B+		14/03/2012	19/03/2012	+5	+34
17	R33	K B+		14/03/2012	20/03/2012	+6	+35
18	R58	K B+		17/04/2012	23/04/2012	+7	+40
19	R59	K B+		17/04/2012	18/04/2012	+1	+35
20	R62	K B+		17/04/2012	19/04/2012	+2	+36
21	R64	K B+		17/04/2012	23/04/2012	+6	+40
22	R69	NB+		21.05.2012	29.05.2012	+8	-
23	R71	NB+		21.05.2012	29.05.2012	+8	-
24	R72	NB+		23.05.2012	vivo		-
25	R73	NB+		23.05.2012	vivo		-
26	R74	NB+		04.06.2012	vivo		-
27	R75	NB+		04.06.2012	12.06.2012	+8	-
28	R76	NB+		04.06.2012	12.06.2012	+8	-
29	R77			11.06.2012	vivo		-
30	R78			11.06.2012	13.06.2012	+2	-
31	R79			11.06.2012	13.06.2012	+2	-

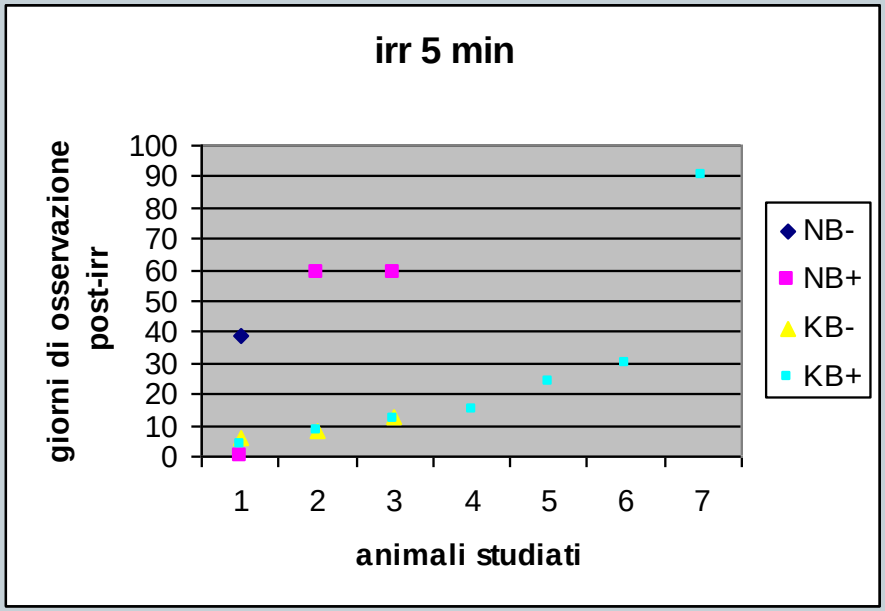
N = normal tissue
K = neoplastic tissue
B- = irradiation without BPA administration
B+ = irradiation with BPA administration

Summary of the Irradiation Schemes

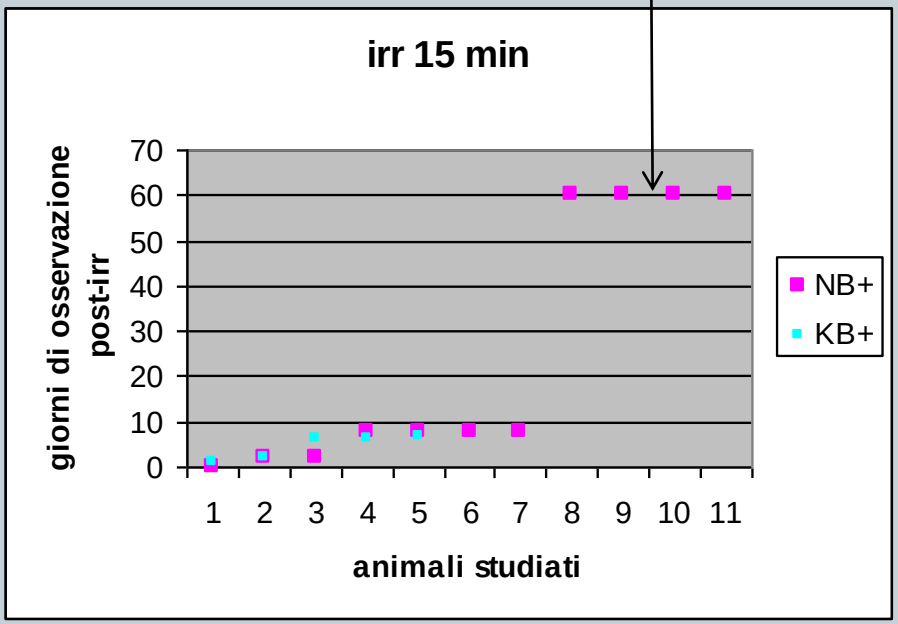
	NB-	NB+	Total rats N	KB-	KB+	Total rats K	Total rats
5 min	1	3	4	3	7	10	14
10 min					1	1	1
15 min	0	11	11	0	5	5	16

N = normal tissue
K = neoplastic tissue
B- = irradiation without BPA administration
B+ = irradiation with BPA administration

Times of observation or sacrifice in order to obtain specimens for the histological analysis



Still alive

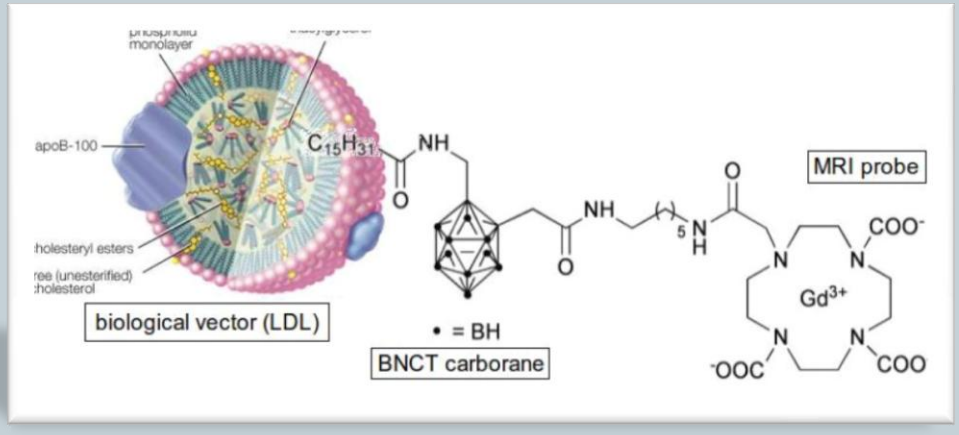


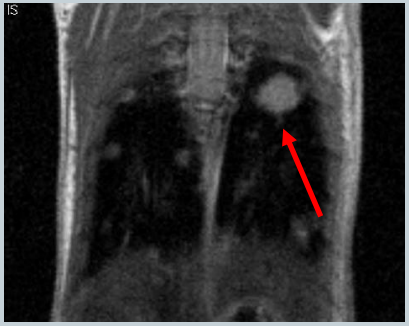
Goals

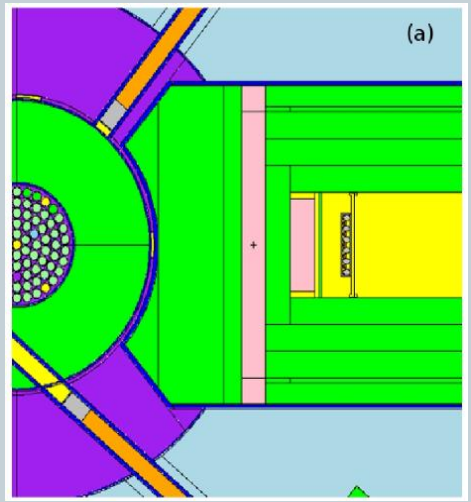
- Study the toxicity of the normal tissues due to neutron irradiation alone and BNCT treatment
- Study the effect of BNCT in reducing the lung metastases

For these aims, bioptic specimens of lung, heart, skin, liver, stomach, intestine, kidneys and medula have been taken and prepared for the histological analysis that are being performed by radiobiologists of University of Florence.

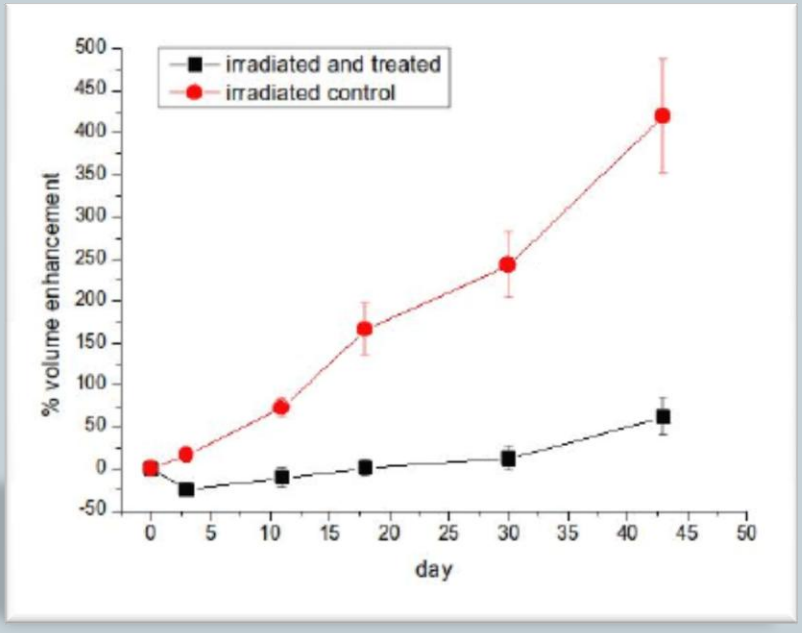
Irradiation of mice from UniTo with a new carrier





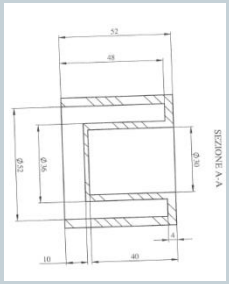


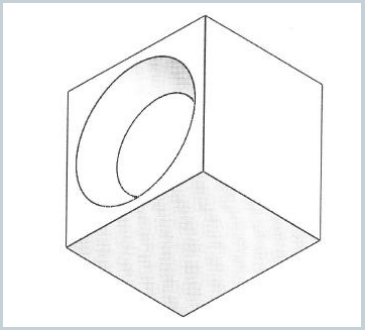
The Results

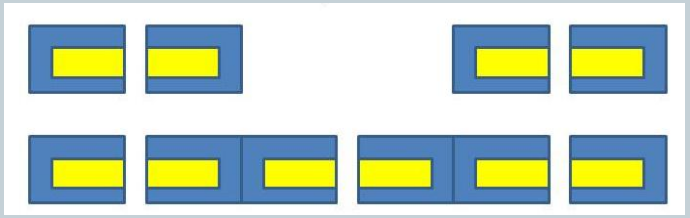

irradiated and treated
irradiated control
% volume enhancement
day
500
450
400
350
300
250
200
150
100
50
0
-50
0
5
10
15
20
25
30
35
40
45
50

New shielding

- 5 geometrical boxes filled with lithium carbonate, manufactured @ our workshop.





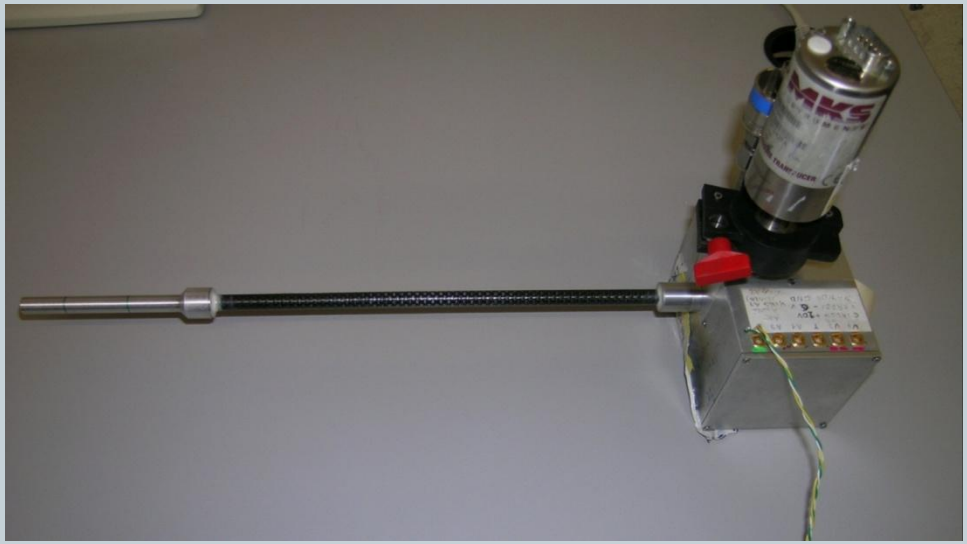


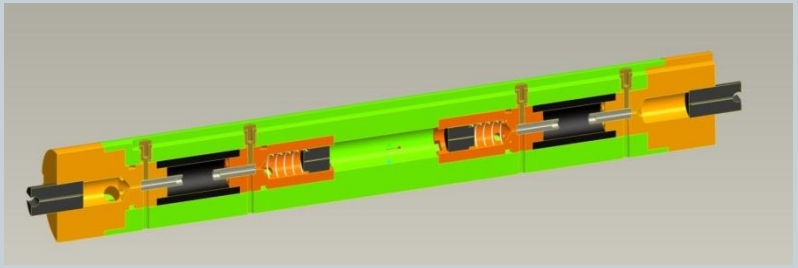
- 1° irradiation of mice with the new shielding: tomorrow (dose escalation to set the limits for the normal tissues)
- Dose escalation in order to block the tumor growth

2. Uptake measurement in patients

- Still, no active protocol, but:
- Letter of intent by HUCH (Leena Kankaanranta)
- Letter of intent from Catanzaro (prof.Gasperini)
- Project for BPA-F18 test in patient approved at IOV (Laura Evangelista). Funded by Ministry of Health last month, with the participation of S.Altieri and S.Bortolussi. A proptocol for patients will be soon available for skin recurrences of breast cancer and thus it will be possible to extend also to lung
- Collaboration with Prof.Luisetti and Dr. Giulia Stella, pneumologists of S.Matteo hospital and Candiolo Oncological Center for the study of an animal model with human mesothelioma and thoracic cancer.

In collaboration with Legnano group





New measurements with the Twin TEPC to characterize the thermal column of the TRIGA Reactor from the point of view of microdosimetry.
Next measurement scheduled for the first week of July.
Characterization of the borated walls of the microdosimeter
By means of alpha spectrometry and neutron autoradiography

Invitations

- Dr Rubèn O. Farias, Mario A.Gadan and Sara J.Gonzalez from Comisiòn Nacional de Energìa Atomica, Buenos Aires, Argentina
- Dr.Ing. David W.Nigg from Idaho National Laboratories, Idaho, USA
- Leena Kankaanranta, HUCH, Helsinki, (clinical BNCT research)

Publications

- S.Bortolussi, J.G.Bakeine, F.Ballarini, P.Bruschi, M.A.Gadan, N.Protti, S. Stella, A.Clerici, C.Ferrari, L.Cansolino, C.Zonta, A.Zonta, R.Nano and S.Altieri, “Boron uptake measurements in a rat model for Boron Neutron Capture Therapy of lung tumours”, Appl. Rad. Isot., 69 (2011) 394–398
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- S. Bortolussi, J.M. Pinto, S.I. Thorp, R.O. Farias, M.S. Soto, M. Sztejnberg, E. C.C. Pozzi, S. Gonzalez, M.A. Gadan, A.N. Bellino, J. Quintana, S. Altieri and M. Miller, “Simulation of the neutron flux in the irradiation facility at RA-3 reactor”, Appl. Rad. Isotop., 69(12), 2011, 1924–1927
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- F.Ballarini, J.Bakeine, S.Bortolussi, P.Bruschi, L.Cansolino, A.M.Clerici, C.Ferrari, N.Protti, S.Stella, A.Zonta, C.Zonta and S.Altieri, “Cell death following BNCT: a theoretical approach based on Monte Carlo simulations”, Appl. Rad. Isotop., Appl. Rad. Isotop., 69(12). 2011, 1745-1747

Publications

- S.Geninatti-Crich, D.Alberti, I. Szabo, A. Deagostino, A. Toppino, A. Barge, F. Ballarini, S. Bortolussi, P.Bruschi, N.Protti, S. Stella, S. Altieri, P. Venturello, S.Aime, "Magnetic Resonance Imaging guided Neutron Capture Therapy by a dual Gd/B agent targeted to tumor cells via upregulated LDL transporters" CHEMISTRY-A EUROPEAN JOURNAL, 17(30), 8479–8486, 2011
- C. Schutz, C. Brochhausen, S. Altieri, K. Bartholomew, S. Bortolussi, F. Enzmann , D. Gabel, G. Hampel, C.J. Kirkpatrick, J.V. Kratz, S. Minouchehr , H. Schmidberger, G. Otto "Boron determination in liver tissue by combining Quantitative Neutron Capture Radiography (QNCR) and histological analysis for BNCT treatment planning at the TRIGA Mainz", Radiat Res. 2011 176(3) 388-96.
- Sabrina Stella, Francesca Ballarini, Silva Bortolussi, Piero Bruschi, Nicoletta Protti and Saverio Altieri, "Design of a facility for boron measurement based on prompt gamma neutron activation analysis", The front edge of BNCT development, proceedings of Young Members BNCT Meeting, Hsue, Taiwan, 3-8 December 2011, pp. 236-244
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