The title of the presentation is: Neutron production with clinical LINACs for BNCT studies in physical, medical and biological fields.
Neutron production with clinical e-LINAC’s is achieved by in-hospital electron Linear Accelerators, normally devoted to radiotherapy, Using a photo-neutron \((\gamma,n)\) converter © Patented by Trieste University in 2004. The project was also funded by INFN [PhoNeS (PhotoNeutron Source 2005-2006), NOE2(Deceleroni per Organi Espiantati 2009-2010)] and Italian National Research Program PRIN05 (2006-2007).
Neutrons are produced by Giant Dipole Resonace of photons on High Z nuclei.
The neutron production yield on lead, above 15 MeV electron energy, can be of the order of \( Y_n \sim 10^{12} \text{ s}^{-1} \text{ kW}^{-1} \) with an efficiency approaching 1% n/e.
The PhonNeS project has allowed to build simple prototypes easy to install and operate at existing clinical Linacs which in the future, once optimized for dedicated Linacs, can be used for BNCT inside radiotherapy hospital departments.
Three prototypes have already been built, currently providing thermal/epithermal neutron flux of more than $10^7 \text{n cm}^{-2} \text{s}^{-1}$. With future developments fluxes of the order of $10^9 \text{n cm}^{-2} \text{s}^{-1}$ are expected.
The first three prototypes have been successfully tested with nine radiotherapy Linacs of hospitals in Italy and Austria.
The moderated neutron spectra have been measured and compared with simulations, showing the good expected shape.
The relevant thermal peak has clearly been observed and compared with nuclear reactor data.
One of the main current applications is in biological studies for determining B-10 concentration in samples of resected organs, perfused with Boron-10 carriers like $^{10}$Boron-Phenyl-Alanine (BPA).
BPA was perfused for more than two hours in human lungs resected, being affected by adenocarcinoma or pleural mesothelioma.
After perfusion, lung tissue samples were prepared using a Leica Cryostat and deposited on CR39 track etch detectors.
The CR39 plastic track etch detectors are subject to polymer chain breaks due to passage of high LET fission products of B-10 neutron capture.

The following chemical etching procedure transforms the defects in the polymeric structure in approximately 10 micron wide holes easy to see, measure and count at the microscope.
The new method was applied to human lung resected pulmonary lobe affected by non-small cell lung cancer at S. Luigi d’Orbassano Hospital in Turin (Italy).
Pictures showing the various steps of the photo-neutron source installation and operation in front of Elekta SLIT 25 MV radiotherapy e-LINAC at Turin “Le Molinette” Hospital in December 2007. The last picture shows lung tissue samples between two CR-39 layers (37 x 13 x 1 mm$^3$) irradiated with hyperthermal neutrons in the PhoNeS cavity.
The samples, deposited on CR39 track etch detectors, have been irradiated in the PhoNeS cavity, in front of an Electa SL25 25 MV radiotherapy Linac, integrating 70000 M.U. @400 M.U./min, for ~$10^4$ s (~3 hours), corresponding to a fluence of ~$10^{11}$ n/cm².
The microscope digital images have been processed by Image-Pro Plus © Microscopic Image Automated Analysis software for hole area study and counting.
The CR39, etched after the irradiation, show the same features of the corresponding tissue samples encoding in the hole density the B-10 concentration.
The advantage of the method is also the possibility to compare with the images of the adjacent samples prepared for the histological analysis.
The B-10 concentration can be compared to the various features of the tissue in the samples.
Relevant areas of the samples can be looked at the microscope with larger magnification in order to recognize tissue or tumor cells features.
Tumor cells are clearly visible.
Boron-10 concentration in healthy tissue is less than 30 ppm.
Boron-10 concentration in tumor tissue is higher, on average of the order 40 ppm.
This slide shows the colored histological samples on which the microscopic analysis can be performed at the desired magnification.
Etched CR39 images compared to sample images for the latest irradiation in 2009.
The etched CR39 samples have been processed and color coded for the determination of B-10 concentration in various areas of the tissues.
The software chain of programs used (ImageJ, Cinema 4D, Surfer8) has allowed to indicate which areas of the samples have the highest B-10 concentration.
The microscope images of the different tissue area clearly show the different type of tissue: tumor versus healthy.
Also the magnified images of the cells show they are very different according to being tumor or healthy cells.
A new way of doing Neutron Autoradiography with microstrip silicon detectors has been performed at the S.Anna hospital in Como again by irradiating with radiotherapy Linac produced thermal neutrons.
The silicon microstrip detector can be operated in real time during the neutron irradiation, thanks to a very sophisticated electronics based on VLSI ASICs.
The Como method was used for measuring kinetic curves of B-10 concentration in urine samples to be compared with results of Mass Spectroscopy.
The Como method was also used for measuring kinetic curves of B-10 concentration in blood samples and again compared with the corresponding results of Mass Spectroscopy.
Blood drops were also deposited on CR39 track etch detectors and irradiated with neutrons in the PhoNeS cavity.
Boron-10 concentration was measured with the same procedure of hole density counting applied to the irradiated and etched CR39’s.
The highest B-10 concentration was observed the beginning of perfusion, decreasing afterwards.
The graph shows the results obtained, on the blood samples of one of the lung perfusions, with three different methods: ICP-MS in Pavia, CR39 track etch detectors in Trieste and Si microstrip detectors in Como, by various members of the multicentric PhoNeS/NOE2 collaboration.
Conclusions

- First available in hospital “user friendly” neutron production facility
- First studies of human lung tumor by ex-vivo $^{10}$BPA perfusion
- $^{10}$BPA perfusion in lungs reaches equilibrium in ~ 2hr
- $^{10}$BPA concentration ratio $C_t/C_H$ ~1.5-3 depending on exactly where
- Work in progress in multidisciplinary collaboration
- Activity at dedicated e-LINAC soon
- New High Power e-LINAC next

Thank you
The last slide presents the members of the PhoNeS/NOE2 collaboration.