A least absolute shrinkage and selection operator (LASSO) method was used for feature selection. Model performance was evaluated using Harrell's concordance-index (c-index).
Fitted model included sum entropy (GLCM), high intensity large area emphasis (GLSZM), volume with a minimum relative intensity of 60% of the maximum SUV – AVRI60% (IVH), grey level non-uniformity and long run emphasis (RLGL) and volume (shape) – Table 1. Internal performance of the model was 0.64 ($p<0.01$), while externally it achieved a performance of 0.61 ($p = 0.05$) and 0.58 (0.20), with no further calibration done. Maximum and mean SUV had a univariable performance in the training data of 0.51 and 0.55, respectively.
The reduced accuracy of the model validation can be associated with dissimilarities among data, particularly the different timing and delivered dose of the second scan. Nevertheless, we do see benefit on a timely assessment of response to radiotherapy using the described imaging analysis, particularly when compared with the limited capacity of humans to infer accurate predictions and risk groups identification (*5*). From the Radiomics analysis one can optimally benefit from early response metrics based on changes in metabolism measured with FDG-PET, even before anatomic changes become noticeable, while treatment can still be adapted.
We developed and validated a predictive model on the percentage variation of Radiomics features, the so-called "Delta Radiomics" concept, from repeated FDG-PET scans of NSCLC patients.

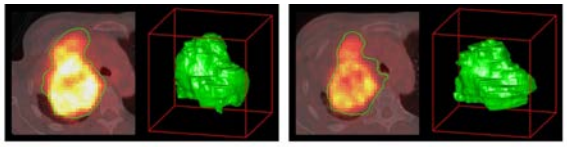

Figure 1 - Example of a pre-treatment (left) and during radiotherapy (right) PET-CT scan of a NSCLC patients from the development dataset.
Table 1 - Developed model after LASSO feature selection on the training dataset. Hazard ratios (HR) and corresponding p-value are presented for the final model. Performance is expressed as the concordance-index (c-index) both internally as for the two validation datasets.

Features	HR	p-value	Internal c-index	Validation c-index 1	Validation c-index 2
Shape – Volume	0.99	0.18			
RLGL – Grey level non-uniformity	1.01	0.02			
RLGL – Long run emphasis	0.98	0.06	0.64	0.61	0.58
GLCM – Sum entropy	0.98	0.20	(p<0.01)	(p=0.05)	(p=0.20)
GLSZM – High intensity large area emphasis	1.00	0.48			
IVH – $AVRI_{60\%}$	1.00	0.50			

Keywords: Early response assessment, non-small cell lung cancer, ^{18}F-FDG-PET imaging, metabolic metrics

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Proton scattering radiography using an emulsion detector: a feasibility study

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Purpose: Proton radiography is an imaging technique in proton therapy giving direct information on the density of the tissues, a useful tool to enhance the precision of proton therapy. It is usually performed as a proton range radiography by measuring the position and the residual range of the protons after the target. The properties of the traversed materials are directly related to multiple scattering so that it is possible to obtain an image through the assessment of the proton angular distribution. This work aims at studying the possibility of performing proton scattering radiography using only one nuclear emulsion film.
Materials and methods: Nuclear emulsion films allow for high-precision tracking of charged particles and, in particular, for reconstructing their angular distribution with a resolution of the order of 1 mrad. Specific detectors for medical applications can be built by interposing double-sided emulsion films with tissue equivalent materials, as it was done for proton range radiography [1] and to study the halo of a proton pencil beam [2]. In the present study, a detector composed by only one emulsion film was exposed to a 138 MeV proton pencil beam at the Gantry 1 at PSI. Two phantoms were placed in front of the detector: the "step" phantom consisted of two different thicknesses of PMMA (3 and 4 cm, respectively); the "rod" phantom had a total thickness of 4.5 cm and contained five aluminum rods (5 × 5 mm^2 section) positioned at different depths in a PMMA structure. Following the chemical development and the automatic microscopic scanning of the emulsion film, proton tracks were identified and their angular distribution reconstructed.
Results: The RMS of the scattering angle was measured for different segmentations of the emulsion film. Areas were chosen as strips parallel to the direction of the step or of the rods, for the first and the second phantom, respectively. To evaluate the resolution, strips of different sizes were considered. As shown in figure 1 (left), the step is clearly identified as a sharp drop of the RMS of the scattering angle. The signal due to the rods is visible as an enhancement of the RMS corresponding to their positions. The rod located nearest to the detector shows a sharper peak while the farthest one appears broader due to the larger distance travelled by the protons. While the contrast for the step phantom is found to be basically the same for range and scattering proton radiography, the signal due to the rods is more evident with respect to what was obtained with proton range radiography [1]. These preliminary results suggest that atomic number plays a fundamental role to increase the contrast of the image.
Conclusions: A feasibility study of proton scattering radiography with a new method based on a single emulsion detector has been performed. The first preliminary results are promising and further studies are under way encompassing in particular Monte Carlo simulations.

Keywords: Proton radiography, proton therapy, nuclear emulsion detectors

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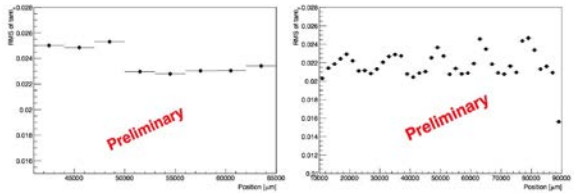

Figure 1 – Proton scattering radiography of a 1 cm PMMA step (left) and of 5x5 mm^2 rods embedded in PPMA (right)

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Development of a track structure detector for biologically weighted treatment planning in particle therapy

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The biological effects of ionizing radiation are determined by the degree of ionization clustering in sensitive biological targets. In Monte Carlo (MC) simulations with geometric DNA models, correlation between the frequency of ionization cluster sizes and resulting clustered DNA damages has been observed [1]. Experimental characterization of radiation track structure on the nanometric scale can be used for assessing biological radiation quality. This approach has important applications in particle therapy, overcoming limitations of the current approach based on rescaling the absorbed dose by the RBE. Measurements of track structure are essential for the validation of MC simulations, which can be applied to patient geometries to produce biologically uniform dose distributions, as recently demonstrated for a simple beam geometry [2]. We are currently developing a compact single-ion gas detector for track structure measurements [3] with applications in clinical particle beams.
The concept of the detector is shown in fig. 1. Radiation-induced positive ions are drifted and focused into the millimetric holes of a THGEM-like structure made of a single-side-clad dielectric plate. Here, ions are accelerated in a strong electric field producing a limited discharge that is spatially restricted to the holes and is confined in time due to the high resistivity of the cathode in contact to the bottom side of the board. Registering the coordinates of the hole position and using the time difference between signals as information on the third dimension, the 3D spatial distribution of the initial ionization events can be reconstructed. Track structure simulations are then used for obtaining scaling factors to convert the spatial distribution of ionizations measured in low-pressure gas to nanoscopic distributions in water [4]. Simulations of track structure for applications to particle therapy were also performed with Geant4-DNA.
Detector characterization has been performed with a ^{241}Am source and low energy alpha and proton microbeams. Ionizations produced in propane and argon gas were detected with single-ion sensitivity. The ion detection efficiency was enhanced by increasing the GEM thickness up to 1 cm, consequently increasing the likelihood of ion impact ionization. Detector dead times of the order several tens of ms strongly affected the detector performance. This is ascribed to the long cathode recharge time. Materials with different resistivity have been tested; however, further work is necessary to find the optimal material. Geant4-DNA simulations showed the feasibility of track structure to produce biologically-weighted particle therapy plans. Assuming that the detector performance can be further improved, it could become an essential tool to validate track-structure-based treatment planning.

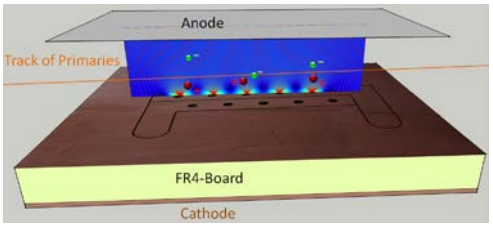

Figure 1: Sketch of one of the detector configurations used in the tests. From the top: anode providing drift field (10 V/cm); low pressure drift region (2-3 mBar of propane or Argon); THGEM (1 cm thickness) with 10 holes of 1.5 mm diameter and top readout electrodes; resistive cathode connected to high voltage (1-2 kV). Electric field lines calculated with COMSOL software are shown.

Keywords: track structure, radiation biological effect, THGEM

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Clinical validation of the M5L lung Computer-Assisted Detection system.

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Lung cancer is one of the leading causes of death in the world. Early diagnosis could be crucial in trying to reduce the mortality: several screening trials, conducted over the last decade in Europe and the US, showed a reduction in 5-year mortality for the branch undergoing chest CT instead of RX [1]. Alongside screening programmes, several Computer-Assisted Detection (CAD) systems were developed, in order to support radiologists in the diagnosis.
The M5L CAD, developed by the INFN in collaboration with CEADEN (Habana, Cuba), is based on a multi-thread approach: it combines the results of two independent algorithms, based on Voxel-Based Neural Analysis (VBNA) [2] and on Virtual Ant Colonies (lungCAM) [3], and provides a framework for further extension to others.
M5L was recently validated on the full LIDC database, the largest publicly available with its 1018 CTs, as well as other datasets (ANODE09, ITALUNG_CT): its sensitivity [4] is about 80% in the 4-6 false positive findings/scan range, which, considering the fact M5L was applied in a clinical-like approach, with no optimization and no data selection, is satisfactory.
Having demonstrated the algorithm generalization capabilities (the training classifier procedure only used 69 of the 1018 LIDC CTs), the development team tackled the issue of making it available to the largest possible user community. Therefore, a Web/Cloud prototype was designed and implemented: CTs are uploaded through a Web front-end interface and analysed by the cloud-backend