The potential of radiomics for radiotherapy individualisation

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In the era of tailored medicine, the field of radiation oncology aims at identifying patients likely to benefit from treatment intensification and of those suffering from undesired treatment-related side-effects. In the past, patient selection in oncology was merely based on, e.g., randomisation, immunohistochemical staining of tumour biopsies, on tumour size or stage, or even on preferences. The introduction and increased availability of high-throughput techniques, such as genomics, metabolomics and Next Generation Sequencing, have revolutionised the field.

In radiation oncology, high-quality anatomical and functional imaging is, besides physical examination, the pillar for target-volume delineation, planning and response assessment. Therefore, ‘radiomics’, referring to the comprehensive quantification of tumour phenotypes through extensive image features analyses, is a logical consequence. Pioneered by the publication of Aerts et al. [1], the field is rapidly evolving regarding techniques, tumour sites and imaging modalities assessed.

In this presentation, the status of radiomics for radiotherapy individualisation will be highlighted and possible areas of future research activities outlined.


OC-0609
Radiomic CT features for evaluation of EGFR and KRAS mutation status in patients with advanced NSCLC

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Purpose or Objective: Molecular profiling is considered standard of care for advanced non-small cell lung cancer (NSCLC) patients. Approximately 25% of adenocarcinoma patients has a KRAS mutation; 10-15% has an activating EGFR mutation where tyrosine kinase inhibitors (TKI) are approved for first line treatment. EGFR and KRAS mutations are mutually exclusive. Obtaining enough tissue for molecular assessment may be difficult. Therefore, in this study we investigated whether EGFR and KRAS mutations can be distinguished from wildtype patients based on features derived from standard CT imaging.

Material and Methods: From a retrospective database of NSCLC patients included between 2004 and 2014, all EGFR-mutated (EGFR+), only exon 19 deletions or exon 21 L858R) patients, the consecutive KRAS-mutated (KRAS+), and EGFR/KRAS wildtype (WT) patients were included. The CT-scan at first diagnosis of NSCLC (i.e., before any treatment) with the primary tumor visible was used for radiomics feature extraction. The primary tumor was delineated using a GrowCut segmentation algorithm (3D Slicer) and manually

SP-0608

New strategies to targeting tumour angiogenesis and hypoxia

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Abstract not received

Symposium with Proffered Papers: Radiomics - the future of radiotherapy?

SP-0606

Imaging-genomics: identifying molecular phenotypes by integrating radiomics and genomics data

To be confirmed

SP-0607

PET/CT heterogeneity quantification through texture analysis: potential role for prognostic and predictive models

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The use of PET/CT has increased much in the last decade, from a purely diagnostic to a radiotherapy planning and therapy monitoring tool. For these new applications, the quantitative and objective exploitation of PET/CT datasets becomes crucial given the well-established limitations of visual and manual analysis. Within this context, the Radiomics approach which consists in extracting large amount of information from multimodal images relies on a complex pipeline: image pre-processing, tumor segmentation, image analysis for shape and heterogeneity features calculation, and machine learning for robust and reliable features selection, ranking and combination with respect to a clinical endpoint. Although the Radiomics approach has been extensively applied to CT imaging, its use for PET/CT is more recent and less mature. There are however already a large body of published works hinting at the potential value of textural features and other advanced image features extracted from PET/CT in numerous tumour types. However, many methodological issues and limitations specific to PET/CT image properties have been highlighted by recent studies. This presentation aims at presenting both the promises and potential of advanced PET/CT image textural features analysis to build prognostic and predictive models, as well as the numerous pitfalls to avoid in order to further advance research in that promising field.

SP-0607

PET/CT heterogeneity quantification through texture analysis: potential role for prognostic and predictive models

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adapted if needed. 724 CT features were calculated using radiomics software. To test if features were different for EGFR+, KRAS+ or WT patients one way ANOVA (initially without correction for multiple testing) was performed using a 5% significance level. A pair-wise comparison (t-test) identified significantly different groups.

Results: 51 EGFR+, 47 KRAS+ and 32 WT patients were included. 41 features were significantly different between EGFR+, KRAS+ and WT patients. One feature is a first order gray-level statistics feature (7% of feature subgroup total), two are gray-level co-occurrence matrix based (9%), two gray-level size-zone matrix based (18%), one Laplacian-of-Gaussian transform based (0.5%) and 35 are wavelet transform based features (7%). Statistics for the significant features are shown in Table 1. One easy to interpret significantly different feature for EGFR+ compared to WT patients was the median Hounsfield Unit (HU). EGFR+ patients had a median HU which is on average 54±23 HU higher compared to WT patients, see Figure 1. KRAS+ patients did not have a significantly different median HU compared to EGFR+ or WT patients.

<table>
<thead>
<tr>
<th>Feature inside primary tumor</th>
<th>EGFR+ Mean ± std</th>
<th>KRAS+ Mean ± std</th>
<th>WT type Mean ± std</th>
<th>Different groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLCM_cccA0.2</td>
<td>0.12 ± 0.04</td>
<td>0.12 ± 0.06</td>
<td>0.12 ± 0.07</td>
<td>EGFR+ vs. both</td>
</tr>
<tr>
<td>GLCM_cccB0.2</td>
<td>0.17 ± 0.13</td>
<td>0.14 ± 0.16</td>
<td>0.14 ± 0.13</td>
<td>EGFR+ vs. both</td>
</tr>
<tr>
<td>GLCM_meanIntensity</td>
<td>3.5 ± 0.20</td>
<td>3.0 ± 0.30</td>
<td>3.4 ± 0.10</td>
<td>EGFR+ vs. WT</td>
</tr>
<tr>
<td>GLCM_varIntensity</td>
<td>3.5 ± 1.07</td>
<td>3.8 ± 1.02</td>
<td>4.5 ± 1.03</td>
<td>EGFR+ vs. WT</td>
</tr>
<tr>
<td>GLCM_varIntensityLocalMean</td>
<td>0.9 ± 0.25</td>
<td>0.8 ± 0.34</td>
<td>0.9 ± 0.35</td>
<td>EGFR+ vs. both</td>
</tr>
<tr>
<td>Median Hounsfield Unit</td>
<td>51 ± 9.69 HU</td>
<td>9.1 ± 12.11 HU</td>
<td>-2.1 ± 11.44 HU</td>
<td>EGFR+ vs. WT</td>
</tr>
</tbody>
</table>

Figure 1: This image shows the difference in intensity between a WT patient (upper, median: 890 HU) and an EGFR+ patient (lower, median 61 HU).

Conclusion: We showed that there are differences in radiomic CT features between EGFR+, KRAS+ and WT NSCLC. The next step will be to externally validate (work in progress) a robust radiomic signature, based on standard CT imaging. Also this allows to monitor radiomic signature evolution under treatment.

Symposium: Radiobiology of proton / carbon / heavy ions

SP-0610 Gene expression alterations to carbon ion and X-irradiation M. Moreels*, K. Konings, S. Baatout†

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Hadr on therapy is an advanced technique in the field of radiotherapy that makes use of charged particles such as protons and carbon ions. The inverted dose-depth profile and the sharp dose fall-off after the Bragg peak offered by charged particle beams allow for a more precise localization of the radiation dosage to the tumor as compared to the conventional used photons. As a consequence, the surrounding healthy tissue receives a much lower dose. Besides this ballistic advantage, the use of high-linear energy transfer (LET) carbon ion beams offers also a biological advantage, i.e. a higher relative biological effectiveness (RBE) as compared to conventional low-LET photon therapy. Carbon ion radiation is thus more effective in inducing DNA damage, cell cycle arrest and cell death, thereby accounting for highly lethal effects, even in tumors that are resistant to X-ray irradiation.

The response of an irradiated cell depends on the dose, dose-rate, radiation quality, the lapse between the radiation-induced stress and the analysis, and the cell type. In this context, genome-wide studies can contribute in exploring differences in signaling pathways and to unravel high-LET-specific genes. Several studies within SCK-CEN and outside have already compared changes in gene expression induced by different radiation qualities. Overall, the number of differentially expressed genes as well as the magnitude of (dose-dependent) gene expression changes was found to be more pronounced after irradiation with particle beams.

Currently, the Radiobiology Unit of SCK-CEN is deeply investigating the effect of low- and high-LET radiation on the gene expression of different cancer cell lines in vitro. Our results clearly demonstrate a dose-dependent downregulation in several genes involved in cell migration and motility after carbon ion irradiation. A higher number of genes as well as more pronounced changes in their expression levels were found after carbon ion irradiation compared to X-rays. Further research are currently investigating whether the observed molecular changes also influence the cellular ‘behavior’ after irradiation in terms of cell migration and motility after irradiation, since these are prominent characteristics of cancer progression and metastasis.

Assessing both the risks and advantages of high-LET irradiation can contribute to the study of the biological effect on the tumor and will lead to further acceptance and improvement of the clinical outcome of hadron therapy.

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SP-0611 Normal tissue response in particle therapy B.S. Sørensen

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Particle therapy as cancer treatment, with either protons or heavier ions, provide a more favourable dose distribution compared to x-rays. While the physical characteristics of particle radiation have been the aim of intense research, less focus has been on the actual biological responses particle irradiation gives rise to. Protons and high LET radiation have a higher radiobiological effect (RBE), but RBE is a complex quantity, depending on both biological and physical parameters. One of the central questions in particle therapy is whether the tumor and the normal tissue has a differential RBE due to the difference in α/β ratio. Most of the data to enlighten this is in vitro data, and there is very limited in