Optimizing *Radiomics* for multimodal medical imaging

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Scientific context

Intratumour heterogeneity has a measurable treatment impact in oncology [1]. Non-invasive imaging can reflect underlying biology and enable assessment of the whole tumour phenotypic heterogeneity [2], [3] whereas sampling of a tumor genotype is typically limited to a small tumour sample (biopsy) [4]. A comprehensive extraction of all available quantitative information contained in multimodal images (CT, MRI, PET/CT) of tumours by extracting various image features including intensity, shape and heterogeneity (popularly known as “*Radiomics*” [5]), would allow building more efficient decision support systems compared to the conventional approaches based mostly on visual/manual characterization of images. With the increased use and applications of imaging in the context of treatment guidance and monitoring, the need for quantification has become crucial. Development of methods for quantitative extraction of biologically and clinically relevant information from multimodal images has been rapid in the recent years, yet has not been sufficiently validated and has not achieved wide acceptance, especially from the clinical community. In addition, this lack of standardization makes the comparison of published results challenging, if not impossible.

Proposed developments

We will specifically address *Radiomics* methodological standardization by implementing a multimodal automated framework and thoroughly investigating the impact of all the involved methodological steps (*i.e.* image segmentation [6], [7] and post-reconstruction processing such as denoising or contrast enhancement [7] , quantization and textural matrices design [8], [9] , shape metrics definition and calculation [10], [11] , fractal and multiscale methodology [12] , etc.). This *Radiomics* framework will be methodologically validated by identifying the most robust, reproducible, reliable, least redundant and most clinically relevant features. In addition, we will investigate its translational clinical value in several types of tumors by building decision support systems in a multicentric setting using large cohorts including 4 types of tumors (head & neck, lung and esophageal with PET/CT, and glioblastoma multiforme with multimodal MRI). The main aims are to: 1. Standardize and improve the robustness of *Radiomics* for multimodal imaging by focusing on solving methodological issues associated with multimodal images and especially a multicentric context. 2. Investigate and validate the ability of determining the most reliable and efficient features or combination of features through machine learning. 3. Exploit the validated framework to identify the most clinically relevant features as a basis to design decision support systems with demonstrators in 4 tumour types, by exploiting available cohorts, and investigate their performances compared to conventional approaches and state-of-the-art prediction tools. We expect the results of this project to lead to the production of guidelines and recommendations that may subsequently translate into the production of more homogeneous and comparable results across studies, in turn leading to a potential paradigm shift in patient management based on multimodal images, from diagnosis and prognosis to treatment monitoring and assessment of response to therapy.

Candidate profile

- Solid theoretical mathematical and/or computer sciences background (Master and/or Engineer level).
- Machine learning and statistics knowledge and proficiency is mandatory.
- Highly proficient in spoken and written English.
- Experience and skills related to image processing and analysis.
- Experience and skills related to medical imaging.

Send a letter of motivation (in English), CV and grades obtained during the cursus to: mathieu.hatt@inserm.fr

References

[1] S. Basu, T. C. Kwee, R. Gatenby, B. Saboury, D. A. Torigian, and A. Alavi, “Evolving role of molecular imaging with PET in detecting and characterizing heterogeneity of cancer tissue at the primary and metastatic sites, a plausible explanation for failed attempts to cure malignant disorders,” *Eur J Nucl Med Mol Imaging*, vol. 38, no. 6, pp. 987–91, Jun. 2011.

[2] H. J. W. L. Aerts, E. R. Velazquez, R. T. H. Leijenaar, C. Parmar, P. Grossmann, S. Cavalho, J. Bussink, R. Monshouwer, B. Haibe-Kains, D. Rietveld, F. Hoebers, M. M. Rietbergen, C. R. Leemans, A. Dekker, J. Quackenbush, R. J. Gillies, and P. Lambin, “Decoding tumour phenotype by noninvasive imaging using a quantitative radiomics approach,” *Nat. Commun.*, vol. 5, p. 4006, 2014.

[3] E. Segal, C. B. Sirlin, C. Ooi, A. S. Adler, J. Gollub, X. Chen, B. K. Chan, G. R. Matcuk, C. T. Barry, H. Y. Chang, and M. D. Kuo, “Decoding global gene expression programs in liver cancer by noninvasive imaging,” *Nat Biotechnol*, vol. 25, no. 6, pp. 675–80, Jun. 2007.

[4] M. Gerlinger, A. J. Rowan, S. Horswell, J. Larkin, D. Endesfelder, E. Gronroos, P. Martinez, N. Matthews, A. Stewart, P. Tarpey, I. Varela, B. Phillimore, S. Begum, N. Q. McDonald, A. Butler, D. Jones, K. Raine, C. Latimer, C. R. Santos, M. Nohadani, A. C. Eklund, B. Spencer-Dene, G. Clark, L. Pickering, G. Stamp, M. Gore, Z. Szallasi, J. Downward, P. A. Futreal, and C. Swanton, “Intratumor heterogeneity and branched evolution revealed by multiregion sequencing,” *N Engl J Med*, vol. 366, no. 10, pp. 883–92, Mar. 2012.

[5] P. Lambin, E. Rios-Velazquez, R. Leijenaar, S. Carvalho, R. G. van Stiphout, P. Granton, C. M. Zegers, R. Gillies, R. Boellard, A. Dekker, and H. J. Aerts, “Radiomics:

extracting more information from medical images using advanced feature analysis," *Eur J Cancer*, vol. 48, no. 4, pp. 441–6, Mar. 2012.

[6] C. Parmar, E. Rios Velazquez, R. Leijenaar, M. Jermoumi, S. Carvalho, R. H. Mak, S. Mitra, B. U. Shankar, R. Kikinis, B. Haibe-Kains, P. Lambin, and H. J. W. L. Aerts, "Robust Radiomics feature quantification using semiautomatic volumetric segmentation," *PloS One*, vol. 9, no. 7, p. e102107, 2014.

[7] M. Hatt, F. Tixier, C. Cheze Le Rest, O. Pradier, and D. Visvikis, "Robustness of intratumour (18)F-FDG PET uptake heterogeneity quantification for therapy response prediction in oesophageal carcinoma," *Eur. J. Nucl. Med. Mol. Imaging*, Jul. 2013.

[8] R. T. H. Leijenaar, G. Nalbantov, S. Carvalho, W. J. C. van Elmpt, E. G. C. Troost, R. Boellaard, H. J. W. L. Aerts, R. J. Gillies, and P. Lambin, "The effect of SUV discretization in quantitative FDG-PET Radiomics: the need for standardized methodology in tumor texture analysis," *Sci. Rep.*, vol. 5, p. 11075, 2015.

[9] M.-C. Desseroit, C. Cheze Le Rest, F. Tixier, M. Majdoub, R. Guillevin, R. Perdrisot, D. Visvikis, and M. Hatt, "Complementary Prognostic Value of CT and 18F-FDG PET Non-Small Cell Lung Cancer Tumor Heterogeneity Features Quantified Trough Texture Analysis," *American Association of Physicists in Medicine annual meeting - Science Council session*, 2014.

[10] O. Grove, A. E. Berglund, M. B. Schabath, H. J. W. L. Aerts, A. Dekker, H. Wang, E. R. Velazquez, P. Lambin, Y. Gu, Y. Balagurunathan, E. Eikman, R. A. Gatenby, S. Eschrich, and R. J. Gillies, "Quantitative computed tomographic descriptors associate tumor shape complexity and intratumor heterogeneity with prognosis in lung adenocarcinoma," *PloS One*, vol. 10, no. 3, p. e0118261, 2015.

[11] M. Majdoub, C. C. L. Rest, P. Lambin, R. Larue, L. Quero, L. Vercellino, B. Hoeben, E. Visser, D. Visvikis, and M. Hatt, "Assessing prognostic value of 18F-FDG PET derived

functional shape features," *J. Nucl. Med.*, vol. 56, no. supplement 3, pp. 446–446, May 2015.

[12] F. Michallek and M. Dewey, "Fractal analysis in radiological and nuclear medicine perfusion imaging: a systematic review," *Eur. Radiol.*, vol. 24, no. 1, pp. 60–69, Jan. 2014.