



Deployment of Artificial Intelligence for Assessment of Response to Systemic Therapies in Colorectal Cancer

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Colorectal cancer is one of the leading causes of cancer worldwide, accounting for over 25% of cancers and 35% of cancer-related deaths across the globe [1,2]. Liver metastases present in more than half of colorectal cancer cases [3]. Therefore, personalized therapy and evaluation of changes in tumor size are pivotal for treatment success [4]. To this end, the response assessment to systemic therapies primarily relies on using the Response Evaluation Criteria in Solid Tumors (RECIST). RECIST relies solely on anatomical information regarding tumor size [5]. In general, tumor therapy success is measured by radiographic markers to predict overall survival. Newer therapies require new predictors for response to treatment, which can be developed by data computed from large CT scan databases [4].

Combination of Radiomics features using AI

Radiomics is a technique that allows for extraction of quantitative features from medical images. It can provide alternative noninvasive measures in the detection, differentiation, and prognosis of patients undergoing treatment [6]. Machine learning enables the automated mining of quantitative features, which allows the discovery of combinations of certain features (typically referred to as signatures) to predict outcomes of interest, such as patients' survival after treatment initiation [4]. Quantitative features are, for instance, tumor volume (better indication of tumor size), tumor shape (more irregular borders indicate more aggressive tumors), and heterogeneity of tumor density (a representation of tumor vascularity and necrosis) [5]. New machine learning algorithms can predict time to death as a continuous variable, unlike RECIST, which converts continuous



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variables of maximum lesion diameter into categories [4].

With the help of the Support vector regression algorithm the length of stay has been predicted with an accuracy of 83% [7]. Bi-directional long short-term memory (BI-LSTM) model has been utilized to predict readmission with an accuracy of 80-96% [8].

Liver metastases develop in a significant proportion of patients during the follow up period [9]. Early identification of the subgroup of patients who can be cured by surgical resection of metastases can lead to superior outcome. Hepatic metastases are typically best seen in portal venous phase of contrast CT where they appear as hypodense lesions. Lesion conspicuous depends on differential enhancement between metastatic lesions and the adjacent parenchyma. Some hypervascular lesions may show significant arterial enhancement during the arterial phase.

A fully automatic Deep Learning-based convolutional neural networks (DL CNN) has helped in recognizing optimal portal venous phase acquisitions [10].

TNM staging plays an essential role in the multifaceted treatment approach. With the use of CNN algorithm AI has been shown to be useful in differentiating T2 and T3 tumors with an accuracy of 94% [11].

Prediction of toxicity (chemotherapy, targeted agents, immunotherapy)

A growing field of research is leveraging AI to empower new prognostic, predictive, and therapeutic approaches in patients treated with immunotherapy, chemotherapy, and targeted agents [12]. To guide modern clinical decisions, we should decrease our dependence on size-based categories and reconceptualize progression as a spectrum from acceleration to deceleration [12]. One example of this is metabolic PET imaging, which may have an advantage over CT in evaluating immune-related adverse events (irAE) due to inflammatory processes induced by colitis, pancreatitis amongst others are associated with markedly increased 18F-Fluorodeoxyglucose (FDG) uptake [12]. In addition, high glucose uptake in non-tumoral hematopoietic tissue is typically related to cancer-related systemic immunosuppression and unfavorable outcome. Therefore, glucose metabolism in malignancies can help suggest additional therapies [12].

Prediction of response to chemotherapy

Metastatic colorectal cancer remains incurable; however, with advances in cytotoxic chemotherapy, survival has improved [13]. In rectal cancers, MRI plays a crucial role in identifying desirable patients for chemotherapy. There has been some success with using algorithms to distinguish the lymph node staging N0 from N1-2 patients with moderately strong sensitivities and specificities, in addition to predicting nodal pathology following neoadjuvant chemotherapy. Tumor grade, mutation status, and overall survival were significantly associated with CT-derived texture features of colorectal liver metastasis before the initiation of treatment. The proportion between lesion texture and the surrounding liver may reflect tumor aggressiveness, chemotherapy response, and OS [14].

Prediction of response to targeted agents

In colorectal cancer and other tumors, anti-epidermal growth factor (EGFR) therapies, including tyrosine kinase inhibitors and monoclonal antibodies, demonstrate activity (what do you mean by activity) [3]. In metastatic colorectal cancer,

the evaluation of anti-EGFR monoclonal antibodies relies on CT scan response endpoints [3]. As the decision to continue EGFR-targeted therapies must weigh the risks and potential rewards, there is a strong need for biomarkers that can trace and estimate the likelihood of clinical benefits in each individual patient [3]. There are proof of concept studies demonstrating that machine learning can create signatures which quantify early change in tumor phenotype between baseline and eight weeks post-immunotherapy through CT scan images to predict clinical outcome [3]. Radiomics can help identify statistically significant associations between variables such as clinical outcomes or tumor mutation status through machine learning [3]. In addition, Radiomics can help identify neovascular patterns associated with reduced treatment efficacy, poor outcomes because of reduced drug activity, hypoxia, and promotion of immune evasion, tumor progression, and metastasis [3]. A benefit of AI techniques is that it allows objective and reproducible analysis, which is not apparent to the human eye [3]. Furthermore, since CT scans are widely used, AI can be a cost-effective method for identifying EGFR-resistant tumors due to the clonal acquisition of resistant mechanisms [3].

Prediction of response to immunotherapy

Cancer imaging has historically focused on tumor cells. Still, their immune state, defined by the density, composition, functional state, and organization of tumor-infiltrating leukocytes, may give us more information on the efficacy of immunotherapy and overall prognosis [12]. As radiomic signatures are finetuned and used in larger cohorts, they can eventually guide clinical decisions, such as changing therapies at appropriate times [15]. These signatures are considered noninvasive in vivo surrogates of biological changes post-treatment, understood by both radiologists and oncologists [15]. Computers excel at mining and extracting large amounts of data from quantitative CT analysis, which help predict treatment sensitivity [15]. AI-derived systems are a cost-effective method that can aid clinicians in early predicting treatment efficacy using conventional CT scans [3]. This will allow for more accurate treatment decision-making, which can initiate the foundation for implementing adapted treatment guided by quantitative CT scan interpretation [15]. Progress in immunotherapy imaging has given us both the complex patterns of immunotherapy and the capacity to train AI to discover the complex relationships of imaging features [12].

Conclusion

By objectively assessing medical images and analyzing for clinically relevant features, such as tumor heterogeneity, radiomics can potentially noninvasively individualize medical treatments by detecting patients who will derive long-term benefits from the drug [14,16]. With the advent of technological advancements, radiomics provides a promising potential role in the diagnosis and personalized treatment of colorectal cancer. Although AI in medicine is still beginning, this technology has significant benefits and promises to boost clinical efficacy, individualize medical decision-making, and improve patient care.

Conflict of interest statement

Conflicts of interest Authors have no conflicts of interest to declare.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and

- mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2018; 68: 394-424.
2. Arnold M, Abnet CC, Neale RE, Vignat J, Giovannucci EL, et al. Global Burden of 5 Major Types of Gastrointestinal Cancer. *Gastroenterology.* 2020; 159: 335-49.e15.
 3. Dercle L, Lu L, Schwartz LH, Qian M, Tejpar S, et al. Radiomics Response Signature for Identification of Metastatic Colorectal Cancer Sensitive to Therapies Targeting EGFR Pathway. *J Natl Cancer Inst.* 2020; 112: 902-912.
 4. Dercle L, Zhao B, Gönen M, Moskowitz CS, Connors DE, et al. An imaging signature to predict outcome in metastatic colorectal cancer using routine computed tomography scans. *Eur J Cancer.* 2022; 161: 138-147.
 5. Dercle L, Zhao B, Gönen M, Moskowitz CS, Firas A, et al. Early Readout on Overall Survival of Patients With Melanoma Treated With Immunotherapy Using a Novel Imaging Analysis. *JAMA Oncol.* 2022; 8: 385-392.
 6. Lambin P, Rios-Velazquez E, Leijenaar R, Carvalho S, van Stiphout RGPM, et al. Radiomics: extracting more information from medical images using advanced feature analysis. *Eur J Cancer.* 2012; 48: 441-446.
 7. Masum S, Hopgood A, Stefan S, Flashman K, Khan J. Data analytics and artificial intelligence in predicting length of stay, re-admission, and mortality: a population-based study of surgical management of colorectal cancer. *Discov Oncol.* 2022; 13: 11.
 8. Anteby R, Horesh N, Soffer S, Zager Y, Barash Y, et al. Deep learning visual analysis in laparoscopic surgery: a systematic review and diagnostic test accuracy meta-analysis. *Surg Endosc.* 2021; 35: 1521-1533.
 9. Hackl C, Neumann P, Gerken M, Loss M, Klinkhammer-Schalke M, et al. Treatment of colorectal liver metastases in Germany: a ten-year population-based analysis of 5772 cases of primary colorectal adenocarcinoma. *BMC Cancer.* 2014; 14: 810.
 10. Ma J, Dercle L, Lichtenstein P, Wang D, Chen A, Zhu J, et al. Automated Identification of Optimal Portal Venous Phase Timing with Convolutional Neural Networks. *Acad Radiol.* 2020; 27: e10-8.
 11. Kim J, Oh JE, Lee J, Kim MJ, Hur BY, et al. Rectal cancer: Toward fully automatic discrimination of T2 and T3 rectal cancers using deep convolutional neural network. *Int J Imaging Syst Technol.* 2019; 29: 247-259.
 12. Dercle L, Sun S, Seban RD, Mekki A, Sun R, Tselikas L, et al. Emerging and Evolving Concepts in Cancer Immunotherapy Imaging. *Radiology.* 2023; 306: 32-46.
 13. Modest DP, Pant S, Sartore-Bianchi A. Treatment sequencing in metastatic colorectal cancer. *Eur J Cancer.* 2019; 109: 70-83.
 14. Tabari A, Chan SM, Omar OMF, Iqbal SI, Gee MS, Daye D. Role of Machine Learning in Precision Oncology: Applications in Gastrointestinal Cancers. *Cancers.* 2022; 15.
 15. Dercle L, Fronheiser M, Lu L, Du S, Hayes W, Leung DK, et al. Identification of Non-Small Cell Lung Cancer Sensitive to Systemic Cancer Therapies Using Radiomics. *Clin Cancer Res.* 2020; 26: 2151-2162.
 16. Wesdorp NJ, Hellingman T, Jansma EP, van Waesberghe JHTM, Boellaard R, et al. Advanced analytics and artificial intelligence in gastrointestinal cancer: a systematic review of radiomics predicting response to treatment. *Eur J Nucl Med Mol Imaging.* 2021; 48: 1785-1794.