

ReSTAGE

Integrative Decision Making in Rectal Cancer Care: Advanced Imaging, Predictive Models, and Patient-Centered Digital Tools

KEYWORDS

Rectal cancer, Response to neoadjuvant chemoradiation therapy, Watch and wait, Magnetic Resonance Imaging, Tissue microstructure, Machine learning prediction models, Digital tools

DURATION

36 months

ABSTRACT

ReSTAGE will transform clinical management of patients with rectal cancer by developing tools capable of accurately and robustly assessing response to neoadjuvant therapy, based on recent advances in Magnetic Resonance Imaging (MRI) and machine learning prediction models, focusing on patient-centered digital tools and information sharing between scientists, clinicians and patients across Europe. Colorectal cancer has the second highest incidence and mortality rates in Europe, with ~30% of tumors located in the rectum. Rectal cancer management has changed in the last years based on recent treatment advances, with imaging playing a crucial role in decision making. Although overall patient outcomes are improving, they vary two-fold across Europe. This may not only be explained by differences in risk factors and screening, but also in diagnosis and management, both highly dependent on imaging. Standard treatment is neoadjuvant chemoradiotherapy (NAT) followed by radical surgery. Given that in 10-40% of cases the surgical specimen shows no signs of viable tumour. i.e. pathologic complete response (pCR), and that radical surgery is highly mutilating and morbid in a significant proportion of patients, there is a rising interest in avoiding it when pCR is expected. Thus, non-operative management as Watch-and-Wait (W&W) programmes based on clinical and MRI evaluation after NAT have risen in popularity across the world. On the other hand, delaying surgery in incomplete responders may lead to worse disease-free survival. Current clinical guidelines recommend re-staging MRI after NAT with response evaluation based on visual analysis by radiologists (e.g. MR-tumour regression grading and similar 3-point ordinal scales, diffusion weighted contrast, split scar sign), but results are disappointing, generally due to low sensitivity and high inter-observer variability. New imaging biomarkers with high predictive power for NAT response are therefore needed to support timely decision-making, and select the right patients for W&W. To address this urgent need and reduce the geographical disparity in treatment outcomes across Europe, ReSTAGE imposes the following goals: Objective 1: Development of MRI biomarkers tailored for rectal cancer. Surgical specimens from LARC patients operated at centers including preclinical MRI facilities will be imaged at ultra-high field (9.4 T) with diffusion and relaxometry approaches designed to characterize tissue structure at the cellular scale. By correlating ultra-high resolution MR images with pathology, the acquisition protocol will be optimised to differentiate viable tumour from benign tissue, and then adapted to a clinically feasible acquisition. Objective 2: Prediction of pathological response to NAT. Rectal cancer patients at different centers will be imaged with the proposed MRI protocol at initial staging and restaging following NAT. Machine learning will be employed to predict the probability of pCR (if patients undergo surgery) or the stability of a complete clinical response (in centres that practice W&W), based on MRI, rectoscopy, digital rectal examination and laboratory results.

The integrated model will be prospectively validated, with the long-term goal of selecting patients with low pCR probability for timely surgery, and those with high probability for W&W. Objective 3: Patient-centered digital tools. ReSTAGE will create a data-sharing platform, website, and mobile app to share knowledge, create a teaching and learning environment, and monitor the patients quality of life for different treatment approaches (e.g. surgery vs W&W). Automated translation will enable all patients to access up-to-date clinical information, seek second opinions, and connect with others with similar diagnoses across Europe. ReSTAGE brings together researchers, clinicians and patients to transform rectal cancer management, uniformizing clinical practices and ultimately improving outcomes and quality of life.

PARTNERS

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