

after multimodality treatment of locally advanced rectal carcinoma in the Catharina Hospital in Eindhoven, the Netherlands. The basic treatment principle was preoperative (chemo)radiotherapy, extended surgery and intra-operative radiotherapy (IORT) application to the area most at risk for residual tumor.

Methods: Two-hundred and ninety patients with locally advanced rectal carcinoma who underwent multimodality treatment between 1994 and 2006 were studied. For patients who developed local recurrence, the subsite was classified into presacral, postero-lateral, lateral, anterior, anastomotic or perineal. Patient, treatment and tumor characteristics were related to the subsite of local recurrence.

Results: Thirty-four patients (5-year local recurrence rate: 13.2%) developed local relapse. The most prominent subsite of local recurrence was the presacral subsite; about 40% of all local recurrences. 47% of the local recurrences occurred outside the IORT field. Most recurrences developed when IORT was given dorsally, while least occurred when IORT was given ventrally. Especially after dorsal IORT a high amount of infield recurrences were observed (6 of 8; 75%). In multivariate analysis tumor distance of more than 5 cm from the anal verge and a positive circumferential margin were associated with presacral local recurrence.

Conclusions: Multimodality treatment is effective in the prevention of local recurrence in locally advanced rectal carcinoma. Radicality of the resection is the most important factor influencing local control. IORT application to the area most at risk is feasible and seems more effective in the prevention of local recurrence than application of IORT to the dorsal area. Dorsal tumor location results in unfavourable oncologic results. The mechanism of genesis of the presacral local recurrence is puzzling; several hypotheses speculating its origin are discussed.

Scientific Symposium (Wed, 23 Sep, 09:00–11:00) New imaging approaches to response assessment in childhood cancer

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INVITED

Are current tumour response criteria relevant to the 21st century?

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In children with cancers, improved understanding of the molecular basis of diseases and the development of new targeted treatment offer new hope of cures and more effective treatment for a range of childhood malignancies. Accurate assessment of treatment response is critical as it impacts on the choice of treatment and disease prognosis. To date, the most widely used and accepted method of ascertaining tumour response by imaging, is by comparing the measurements of tumour size before and after treatment. Such approach is crystallised in the Response Criteria in Solid Tumours (RECIST) criteria, which was developed from clinical trials data derived largely from adult populations. Although recently revised to a new version (1.1), potential limitations of the RECIST criteria have to be considered when these are applied to the paediatric population.

It has also long been recognised that size measurement based criteria for defining tumour response may not be accurate surrogates for treatment outcomes, such as the time to progression or disease survival. This is particularly important when considering new molecular targeted therapies, which may produce substantial clinical benefits without causing significant tumour size reduction. Thus, there is an urgent need to develop, validate and qualify new imaging biomarkers that reflect biologically relevant endpoints, which can be applied to measure the effectiveness of new targeted treatments developed out of better understanding of the phenotypic and genotypic expressions of childhood cancers.

Quantitative functional imaging techniques based on radionuclide imaging, positron emission tomography, MR imaging (e.g. dynamic contrast enhanced imaging, dynamic susceptibility contrast enhanced imaging, diffusion-weighted imaging, MR spectroscopy) and CT imaging (perfusion CT) are now widely used in drug development and clinical trials in the adult population. Such functional imaging techniques are now being investigated in children. Of these, MR imaging derived techniques are particularly attractive as they are free from harmful ionising radiation and can thus be safely repeated. Functional imaging studies yield unique quantitative information that reflect changes in tumour pathophysiology, allowing for a more specific assessment of the consequence of anti-tumour treatment. By selecting the most appropriate imaging biomarker for the mode of drug action (e.g. specific receptor blockade or metabolic pathway inhibition, angiogenesis inhibition, cell death, apoptosis, decrease in tumour metabolism), the detection of drug effects and tumour response to treatment could potentially be maximised. Hence, a developed panel of imaging biomarkers may prove critical for the individualised treatment of childhood cancers in the future.

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INVITED

Assessing changes in tumour metabolism using magnetic resonance spectroscopy

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Magnetic resonance spectroscopy (MRS) is a technique which can be readily combined with conventional magnetic resonance imaging to measure the levels of various metabolites, lipids and macromolecules in a specified volume of tissue. The most clinically available form is ¹H MRS which provides a broad metabolite profile with approximately 15 metabolites being quantitated in brain tumours. Due to the comparative ease of performing ¹H MRS in the brain, brain tumours have been the most widely studied tumour group, however, there have also been many studies of prostate cancer and breast tumours. It is well established that ¹H MRS metabolite profiles are a powerful characteristic of brain tumours and the use of ¹H MRS as a non-invasive diagnostic tool is well investigated. The most impressive results have been obtained by coupling ¹H MRS with pattern recognition techniques and large multicentre prospective studies have shown a high level of diagnostic accuracy for many tumour types but a lower accuracy when trying to distinguish between glioblastoma and metastases. Fewer studies have been published in children but small studies indicate that the accuracy is similar. Total choline and mobile lipids have been noted as indicators of tumour aggressiveness and a decrease in choline has been used as an indicator of tumour response to drugs. Similarly, myoinositol correlates with lower grade in gliomas and is a good prognostic marker in pilocytic astrocytomas in children. Animal and cell line studies show particular promise for mobile lipids as early indicators of cell death, however these findings are yet to be verified clinically.

MR spectroscopic imaging allows MRS to be collected from several locations at the same time with a spatial resolution down to 1 cubic cm in the brain using a 1.5T clinical scanner and much higher resolution in the prostate using endorectal coils. Using choline as a marker of active tumour, often as a ratio to another metabolite, has allowed accurate targeting of biopsies and is used commonly in some centres for improving the accuracy of prostate biopsies. MR spectroscopic imaging is also useful for identifying tumour invasion and has detected diffuse tumour outside the regions delineated by conventional MRI. This shows promise in radiotherapy planning.

³¹P MRS can detect phosphorous containing metabolites and phospholipids. It is technically more demanding than ¹H MRS but is useful in certain circumstances. Phosphocholine and glycerophosphocholine can be quantitated individually rather than the combined value usually provided by ¹H MRS. The ratio of these two metabolites is a powerful discriminant of some tumour types such as medulloblastoma and of response to treatment with the phosphocholine/glycerophosphocholine ratio decreasing in responding tumours.

Dynamic Nuclear Polarisation (DNP) is an exciting new technique for the production of tracer metabolites which can be detected by MRS and has the particular advantage that the parent molecule and its metabolites can be detected separately. The first clinical studies of DNP using pyruvate as a marker of apoptosis are about to start.

Review Articles:

References

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INVITED

Diffusion weighted imaging in the evaluation of response in abdominal tumours

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MRI provides several foundations for image contrast, on of which is diffusion-weighted imaging (DWI). With this technique, protons (in essence the hydrogen nuclei of water molecules) contribute to the MR signal if they are relatively stationary, e.g., if confined intracellularly. They contribute to signal loss if they move within the picture volume element (voxel), which is the case when their diffusion is unrestricted, e.g., in the extracellular space of a low-cellularity tissue. In the MR scanner we can apply both stronger and weaker diffusion weighting, and the relative change in signal can be quantified so that we get absolute numbers for the apparent diffusibility within each voxel; this is called ADC (apparent diffusion coefficient).