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**Magnetic Resonance Imaging of soft tissue, bone and non-seminomatous testicular tumors.
MRI evaluation before and after therapy.**

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CHAPTER 8

SUMMARY AND CONCLUSIONS

This thesis describes five prospective studies questioning the value of Magnetic Resonance Imaging (MRI) in the diagnostic and treatment evaluation of soft tissue, bone and non-seminomatous testicular tumors.

What is the value of Magnetic Resonance Imaging compared to Computer Tomography in the preoperative local staging of soft tissue and bone tumors?

Good preoperative evaluation of the nature and dimensions of a soft tissue or bone tumor is of great importance for the treatment of patients and the assessment of their prognosis. It may determine the choice between surgical or non-surgical treatment, but also the choice of a specific combination therapy. Especially when planning a limb-salvage therapy it is important to know not only the histological diagnosis but also the dimensions of the tumor and its relationship to adjacent structures such as joints or neurovascular bundles. Regarding the result of preoperative local staging of soft-tissue tumors, no major differences between MRI and CT could be demonstrated. Both methods correctly reflected the macroscopic tumor dimensions in all cases. The relation to the adjacent structures could in general also be adequately assessed. Minor histological abnormalities, such as micro-calcifications in and at the margin of the tumor are beyond the discriminating powers of both techniques.

In bone tumors the situation is even more difficult. Here, evaluation of the dimensions of the tumor and of the destruction of cortical bone is important with reference to the possible use of osteosynthesis or endoprosthesis. Specifically for this evaluation neither MRI nor CT is adequate. Only in about 50% of the patients could the length of the tumor and consequently the length of bone to be resected be measured adequately. Cortical destruction could be evaluated only poorly, particularly with MRI because of the rapid fall of the magnetic resonance signal. Therefore, conventional roentgenograms and isotope bone scans remain necessary. With regard to assessment of tumor growth in the bone marrow and adjacent structures such as muscles, joints and neurovascular bundles, MRI consistently equalled or exceeded CT. Neither in soft-tissue nor in bone tumors was it possible with either MRI or CT to determine the histologic nature of the tumor reliably.

Accordingly, these two methods of examination cannot replace histological examination of a biopsy specimen.

Although the differences between MRI and CT are often only slight, for the preoperative evaluation of soft tissue and bone tumors MRI is nevertheless preferred. This examination involves no use of harmful ionizing radiation and, compared with CT, gives a sharper contrast between the tumor and its environment, which in some cases makes it possible to avoid angiography. Furthermore, MRI, owing to its multidirectional depiction technique, affords better spatial orientation. Owing to the new three-dimensional color depiction, better contrast and good spatial orientation are at present possible with CT. In principle, these new techniques can be applied to MRI as well. Owing to the fast technical developments, it is a question of time before MRI also offers these choices for practical use.

What is the value of Magnetic Resonance Imaging in assessing in vivo response to neoadjuvant chemotherapy for osteosarcoma of the extremities?

Information about the effect of the neoadjuvant chemotherapy on the size and vitality of an osteosarcoma is crucial for the prognosis and subsequent treatment. This applies not only to the planning of adequate limb-salvage therapy but also to the decision as to the level at which an amputation has to be performed. Until now, evaluation of the effect of chemotherapy was based, with good results, on conventional roentgenograms, CT scans, bone scans and histological examination of bone biopsies or of the resection preparation. MRI both before and after chemotherapy provided good anatomical information on tumor size. Owing to the multidirectional exposures, spatial information was superior to CT. Apart from this good anatomical information, changes in signal intensity within the tumor during chemotherapy were also observed. These changes ranged from partial necrosis, with or without a change in volume, to no response at all. In one of the ten patients, a good histological tumor response (Huvos 4) tallied with the MRI image of total necrosis. A clear increase of the T_2 value was also measured in this case. An inverse correlation was also seen in one patient. In this case, a poor histological response (Huvos 1) corresponded with the MRI picture of progression. In the other eight patients, the histological response was moderate to fair (Huvos 2, 3). In these cases, MRI revealed no response or only partial response. The T_2 value in general did not change. Although distinct changes in the MRI image are observed, these are as yet not very specific. Also, it was not possible to

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quantify these changes using MRI parameters such as the T_2 value. In spite of these uncertainties, the fact that changes in the tumor were observed during chemotherapy demands further investigation. Much research will be needed, however, to find a better correlation between the MRI image and the histological alterations. A combination of MRI and Magnetic Resonance Spectroscopy might be useful for this purpose.

What is the role of Magnetic Resonance Imaging compared to Computer Tomography in the staging and evaluation of the effect of chemotherapy on retroperitoneal metastasized non-seminomatous testicular tumors?

With regard to staging and to the assessment of the effect of chemotherapy of the metastasized non-seminomatous testicular tumor, CT has proved its reliability in the last few years. Nevertheless, this examination still has certain shortcomings. Because of the limited directional exposures, obtaining a good spatial orientation within the retroperitoneum is sometimes difficult. This may create problems in determining the extent of a possible retroperitoneal lymph node dissection after the chemotherapy. Another disadvantage is that patients (in this case mostly young males) during an intensive follow-up are regularly exposed to roentgen irradiation of the entire abdomen. Furthermore, CT provides no information on changes of the metabolism of tumor tissues.

In the staging of retroperitoneal metastasized non-seminomatous testicular tumors MRI was equivalent to CT and laparotomy. Here, MRI offered the advantage of the multidirectional depiction technique. Because of this, it was easy to gain three-dimensional information on residual lesions in the retroperitoneum, which have to be removed after chemotherapy. In the course of the treatment, differently reacting components could be distinguished in the retroperitoneal metastases, especially in the T_2 dominant exposures. Tumors with an embryonal component frequently showed a rapid decrease in tumor size. It was only in the mature teratoma component that a correlation could be found between the changes in the MRI image (general or local increase of the T_2 signal intensity) and a pathological anatomical substrate (increase in water contents). Although during the chemotherapy distinct changes could be observed in the retroperitoneal metastases, it was not possible with MRI to predict the ultimate effect of the chemotherapy. In particular it was impossible to demonstrate vital malignant residual tumor. For good evaluation of the effect of chemotherapy checking of the tumor markers and histological examination of a residual tumor, if any, remain necessary for the time being.

In spite of these shortcomings, MRI is to be preferred in the staging and evaluation of the effect of chemotherapy on retroperitoneal metastasized non-seminomatous testicular tumors because this method involves no use of ionizing radiation in these young patients and gives results equivalent to CT or surgical staging.

FINAL CONCLUSION

Compared with other imaging techniques, Magnetic Resonance Imaging is relatively new. Consequently, the technical possibilities are far from exhausted and clinical experience is far from complete. Nevertheless, in many respects MRI is equivalent or even superior to conventional roentgenography or CT scanning. Also, so far, no adverse effects of MRI have been demonstrated. In osteosarcoma as well as in metastasized non-seminomatous testicular tumor, changes in the tumor in the course of chemotherapy could be observed with MRI. Further research, both clinical and technical, will be needed to find correlations between these changes and the morbid-anatomical lesions. The technical evolution proceeds very fast and, if no adverse effects are found in the future, either, clinical application of Magnetic Resonance holds good prospects.

SAMENVAT

In dit proefschrift worden de mogelijkheden van MRI voor de evaluatie van de effecten van chemotherapie op retroperitoneale metastaserende testiculaire tumoren besproken. Het wordt aanbevolen MRI te gebruiken voor de staging en evaluatie van de effecten van chemotherapie op retroperitoneale metastaserende testiculaire tumoren, omdat deze methode geen gebruik van ioniserende straling vereist en resultaten geeft die equivalent zijn aan die van CT of chirurgische staging.

Welke waarde heeft MRI voor de staging en evaluatie van de effecten van chemotherapie op retroperitoneale metastaserende testiculaire tumoren?

Een goede prognose van de uitkomst van de behandeling van testiculaire tumoren is van groot belang voor de patiënt en de behandelende arts. Het is daarom van belang om de prognose van de uitkomst van de behandeling van testiculaire tumoren te verbeteren. Dit kan worden gedaan door de staging en evaluatie van de effecten van chemotherapie op retroperitoneale metastaserende testiculaire tumoren te verbeteren. MRI is hiervoor een goede optie. Het wordt aanbevolen MRI te gebruiken voor de staging en evaluatie van de effecten van chemotherapie op retroperitoneale metastaserende testiculaire tumoren, omdat deze methode geen gebruik van ioniserende straling vereist en resultaten geeft die equivalent zijn aan die van CT of chirurgische staging.