A journey of skull base chordoma

Chapter 8:

Scientific impact

8.1 Main objective of the research

The overall aim of this thesis was to better understand the clinical, radiological and molecular behaviour of skull base chordoma. This thesis addresses different perspectives of the behaviour of skull base chordoma, with focus on the imaging characteristics, patterns of treatment failure, and molecular biology. This thesis confirms that chordoma tumours that can behave differently between patients. After surgical resection and radiotherapy, most chordoma recur within 10 years. In some patients, recurrences occur within months after treatment, while other patients do not show recurrences at all. This thesis shows that recurrences often occur in the surgical cavity. Our theory is that these recurrences are due to microscopic tumour spill during surgery. These cells do not receive a therapeutic radiation dose. However, not all chordoma show this recurrence pattern. Molecular biology might explain the difference in outcome and recurrence pattern between chordoma patients. However, some key elements are missing in genetic analysis of chordoma patients. Because chordoma arise from embryonic notochordal cells, studying the notochord is essential for understanding the molecular biology of chordoma. Because notochordal cells are usually not present in adult bodies, no methods to isolate this structure were described in literature. In this thesis, a method was developed to isolate notochordal tissue that can be used in gene expression studies.

8.2 Contribution to science and social sectors

Using the method that was described to isolate notochordal tissue, future studies can use notochordal tissue as control tissue to study chordoma. Comparing the molecular biology of malignant chordoma to benign notochord may greatly enhance our understanding of the genetic and epigenetic aberrances that cause this tumour to grown, metastasise and recur. Targeting these aberrances may form the basis of future treatment of chordoma.

This thesis shows that chordoma are a heterogeneous group of tumours, which behave differently between patients. Diagnosis, treatment and follow-up is complex. It is therefore important that this tumour is treated in a tertiary centre with expertise in treatment and follow-up of this tumour. Medical therapy is under investigation and inclusion in these studies should be coordinated by these centres. Social discussion could indicate which centres have sufficient expertise in treatment and follow-up of chordoma. Clustering the knowledge may improve outcome in the future.

8.3 Target groups

This thesis is divided in two parts, which each focus on a different target group. In the first part of the thesis the clinical and radiological aspects are studied, which makes this research relevant for clinicians. We found that recurrences occur more frequently in the surgical cavity than previously thought. This may be relevant for surgeons to adapt surgical techniques to prevent this. Radiologist may focus more on these patterns of recurrence and radiotherapists may adapt the target dose and volume.

The second part of the thesis focuses on improving our understanding of chordoma in the field of molecular biology, which is mainly useful for chordoma researchers. The method that was described to isolate notochordal tissue can be used by researchers to study the molecular biology of the notochord and improve our understanding of chordoma. New insights in molecular biology of chordoma may lead to a better understanding of the clinical behaviour and radiological findings, which is beneficial for physicians as well.

8.4 Informing the target groups about the research results

Chordoma research has long been studied in small research groups. Since the foundation of the chordoma foundation, researchers are collaborating more and research data and funding is collected centrally. Chordoma tissue is distributed by this foundation to improve research. This organisation could also distribute the isolated notochordal tissue. This could be a solution for countries in which the described method cannot be used due to legal issues.

The chordoma foundation also organizes meetings to discuss diagnostic and treatment guidelines in chordoma. These meetings are attended by a multidisciplinary, international group of clinicians who have extensive experience caring for chordoma patients. The goal of this group is to develop and publish consensus guidelines, based on available medical and scientific evidence. The outcome is presented in chordoma global consensus group papers. The results of this thesis could be used as evidence in developing these guidelines. The results of this thesis can also be used in national or local guidelines.