

Diplomarbeit

AGE-DEPENDENT CLOSURE OF CRANIAL GROWTH PLATES

CT and MRI findings of cranial sutures

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Graz, am 31.08.17

Veronika Weiss eh.

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GLOSSARY AND ABBREVIATIONS

OES	objective evaluation score
SES	subjective evaluation score
CT	computed tomography
MRI	magnetic resonance imaging
HU	Hounsfield units
WW	window width
WL	window level
m	male
f	female
mm	millimeters
SE	standard error
n	number of cases
SIV	signal intensity value
dex	dexter = right
sin	sinister = left
vs	versus
resp.	respectively
M	metopic suture
S	sagittal suture
(r)L	(right) lambdoid suture
(l)L	(left) lambdoid suture
SO	sphenoccipital suture
(r)SS	(right) sphenosquamous suture
(l)SS	(left) sphenosquamous suture
(r)OM	(right) occipitomastoid suture
(l)OM	(left) occipitomastoid suture
p	p-value = probability value in statistical testing
LKH-Univ. Klinikum Graz	Landeskrankenhaus-Universitätsklinikum Graz
e.g.	exempli gratia (latin) = for example
ICRP	International Commission on Radiological Protection
ROC	receiver operating characteristic

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ZUSAMMENFASSUNG

Die altersabhängige Fusionierung der Schädelknochen und die Verknöcherung der kranialen Suturen stehen seit dem 16ten Jahrhundert im Diskussions- und Forschungspunkt. Seit knapp einem halben Jahrtausend werden laufend Studien über die Verknöcherungsmuster der Schädelnähte in verschiedenen Bereich wie der Anthropologie, Forensik und Radiologie veröffentlicht. (1–6)

Diese retrospektive Arbeit soll den altersabhängigen Verschluss der kranialen Suturen anhand von Messungen in kranialen CT- und MRI-Dünnschichtaufnahmen zeigen. Hierfür wurde ein objektiver Evaluations-Score (*OES*) aufgestellt, welcher anhand von objektiven Parametern den Verknöcherungsgrad der Suturen mittels Score-Punktesystem beschreibt. Ein subjektiver Evaluations-Score (*SES*) beschrieb dieselben Messpunkte und diente als Vergleich. Insgesamt wurden 99 PatientInnen in 6 Altersgruppen eingeteilt: 0 bis <1, 1 bis <5, 5 bis <10, 10 bis <14, 14 bis <18 und 18-99 Jahre. Es wurden ausgewählte Schädelnähte des Schädeldaches (*Sutura metopica*, *Sutura sagittalis*, *Sutura lambdoidea*) und der Schädelbasis (*Sutura sphenoccipitalis*, *Sutura sphenosquamosa* und *Sutura occipitomastoidea*) mittels Score vermessen. Zusätzlich wurde in den 73 CT-Aufnahmen eine Messung der Suturen-Weite durchgeführt.

In den statistischen Auswertungen der CT-Messungen zeigte sich ein signifikanter Unterschied vom objektiven zum subjektiven Evaluations-Score ($p=0$). Dieses Ergebnis unterstreicht die Notwendigkeit einer auf objektiven Messungen basierenden Methode.

Es ließen sich in den Mittelwerten des totalen Scores, wie auch in den Mittelwerten der Scores der einzelnen Schädelnähte, Unterschiede zwischen den Altersgruppen zeigen. Besonderes Interesse galt dem Vergleich der Jugendlichen im Alter von 14 bis <18 Jahren ($n=19$) zu den Erwachsenen von 18 bis 99 Jahren ($n=24$). Hier zeigte sich in den CT-Messungen ein signifikanter Unterschied im Mittelwert des totalen OES ($p=0$), welcher 201 ± 4 bei den Jugendlichen und 231 ± 1 bei den Erwachsenen ergab. Auch wurden im Mittelwert des Schädeldach-OES ($p=0,013$) und im Mittelwert des Schädelbasis-OES ($p=0$), sowie im Mittelwert des OES einzelner Suturen ($p<0,05$) Unterschiede zwischen Jugendlichen und Erwachsenen aufgezeigt. Die Ergebnisse der MRI-Messungen mit einer Fallzahl von 26 PatientInnen, zeigten im Gruppenvergleich der Mittelwerte des OES der *Sutura metopica* und der Mittelwerte des OES der *Sutura sphenoccipitalis* signifikante Unterschiede ($p<0,05$). Diese waren vergleichbar mit den Resultaten der Verknöcherungsmuster des via CT gemessenen Scores.

Diese Studie konnte signifikante Unterschiede der Suturen-Verknöcherungen in den einzelnen Altersgruppen aufzeigen. Eine retrograde Altersbestimmung eines individuellen Schädels wäre anhand der vorliegenden Daten im Sinne einer Gruppeneinteilung von statistisch stark unterschiedlichen Gruppen möglich.

ABSTRACT

The age-dependent fusion of the cranial bones and the ossification of the cranial sutures have been at the discussion and research point since the 16th century. Studies on the ossification patterns of the sutures have been published in various fields like anthropology, forensics and radiology. (1–6)

This retrospective study is intended to show the age-dependent closure of the cranial sutures by radiological imaging of the skull. For this purpose, an objective evaluation score (*OES*) was established, that describes the ossification of the sutures by a score point system based on objective parameters. A subjective evaluation score (*SES*) described the same measuring areas for subsequent comparison. A total of 99 patients were divided into 6 age groups: 0 to <1 years, 1 to <5 years, 5 to <10 years, 10 to <14 years, 14 to <18 years and 18-99 years. Cranial CT- and MRI- high resolution images were used to measure and score selected sutures of the skull cap (metopic suture, sagittal suture and lambdoid suture) and skull base (sphenoccipital suture, sphenosquamous suture and occipitomastoid suture). In addition, the CT images were used to measure the width of the sutures.

In the statistical evaluations of the CT measurements, there was a significant difference from the objective to the subjective evaluation score ($p=0$). This result underlines the necessity of a method based on measurements.

Significant differences between the age groups could mainly be shown using CT images in the means of total OES, means of skull cap OES and means of skull base OES as well as in means of the suture OES ($p<0,05$).

A special interest was the comparison of adolescents aged 14 to <18 years and adults aged 18 to 99 years. There was a significant difference ($p=0$) revealed between the mean of total OES points of adolescents (201 ± 4) and the mean of total OES of adults (231 ± 1). There was also a difference between adolescents and adults in the mean of the skull cap OES ($p=0,013$) and mean of the skull base OES ($p=0$), as well as in the means of OES of individual sutures ($p<0,05$).

The results of the MRI measurements of 26 patients revealed statistical differences in means of metopic suture OES and sphenoccipital suture OES ($p<0,05$), which showed a similar ossification pattern of these sutures as in CT measurements.

Significant differences in the sutures ossification in the individual age groups were revealed. A retrograde age determination of an individual skull could be made by group allocation using statistically very different groups of this study.

1 INTRODUCTION

This diploma thesis focused on scoring the detection and measurement of the age-dependent closure of human cranial sutures in living individuals via CT and MRI imaging. The aim of this study was not only to show an age-dependent suture closure, but to determine age of a patient by evaluating the ossification of the sutures.

1.1 Evaluation of suture ossification as a method of age determination

The first idea of a progressively fusing of cranial bones appeared about 500 years ago in the 16th century and the age related ossification of the skull and its sutures in the use of age determination is highly discussed ever since. (1,7)

Since age assessments are in the focus of various research fields, such as endocrinology, epidemiology, radiography, forensic anthropology, adding an option of age determination into those work fields was one of the main intentions of this study.(3–6)

Forensic science often deals with identification of unknown individuals or verification of a person's profile. As part of the biological profile, the age assessment is one of the main characteristics in describing a person. (8–10)

Previous studies dealing with age evaluation from cranial suture closing focus mainly on post-mortem forensic examinations of skeletons. (11–15) One reason why “the method of determining age by cranial suture closure has always been more generally used” (...) [is] “because the cranium is frequently the best preserved portion of the recovered skeleton.” (16)

To determine the age of a living individual the radiological assessment of hand bone age is widely used in children and adolescents until the age of 18 years. (3,17)

In forensic science, the assessment of age of skeletons younger than 25 years is more easily with epiphyseal fusion in long bones. (10)

Other methods like evaluation of the fusion of epiphysis of the articular surfaces of pubic centers, the clavicle or of long bones are used as macroscopic examination techniques to estimate the age of an individual. (7)

Microscopic analyses are possible methods in postmortem studies, but they are also valuable as an additional review to radiological assessments. (16,18,19)

The potentiality of age-determination via scoring the ossification of the sutures is in focus of many forensic studies which use mainly subjective macroscopic evaluation for analysis. (8,10,20) These standard methods were often criticized for lack of objectivity and deficiency of quantitative analysis. (21,22)

Also in radiological assessments, subjectivity is often a defining element in describing sutures. (23) On the other hand, due to comprehensive studies on age determination on adult skulls the “macroscopic methods for adult age assessment typically do not provide error rates” (8) , but the accuracy of age estimation “decreases for old age” (15).

There are several methods of describing and scoring the ossification of cranial sutures. One of the main reasons for research is to show the normal development of the skull and to compare it to abnormal or disease related changes. Since there are deviations in normal findings of the suture ossification, the definition of a physiological development needs to include outliers as well. (24–33)

For one thing, the skeleton of adolescents is structuring and growing, but then again, the post-maturation process in adults is a progressive degeneration. Degenerative alterations “are not as easily or as well documented as developmental changes”(8) as they are affected and influenced by various environmental factors and habitual activities in addition to the health status and age level of an individual. (31,34,35)

Most studies based on sutures concentrate on either very young patients or adults. (4,19,31,36–39)

For a better comparison of suture ossification in all ages this study included children, adolescents and adults and the age limit was set from 0 to 99 years. This way the sutures are scored by a single method and can be analyzed more easily.

To comprehend the aim and result of this diploma thesis I want to give a brief overview on the characteristics of human sutures and on cranial CT and MRI imaging.

1.2 Definition of sutures

The term suture originates in the latin word “sutura” and means “seam” or “bone seam”. In human anatomy, the sutures join the cranial skull bones.

1.3 Skeleton connections

Skeleton connections can be classified into two main groups: diarthroses and synarthroses.

1.3.1 Diarthroses

Diarthroses are synovial joints. They consist of two facing articular surfaces moving opponent, an intra-articular space filled with synovia and an articular capsule surrounding the joint.

1.3.2 Synarthroses

Synarthroses are primarily immovable joints and adhere via malleable tissues, such as collagenous fibres or cartilages. They can be classified into four subgroups: syndesmoses, synchondroses, synostoses and symphyses.

Between the skull bones the fixed joints are called sutures.

1.3.2.1 Syndesmoses

Syndesmoses are connected by dense tissue such as collagenous or elastic fibres. They can especially withstand traction forces and at certain areas they serve as muscle origins. Most of sutures are fibrous joints and they consist mainly of collagen with varying thickness.

1.3.2.2 Synchondroses

A synchondrosis connects two bones via hyaline cartilage and can resist most notably compressive forces. Some human synchondroses develop into hemiarthroses by generating synovial fluid between the articular surfaces, other ossify to synostoses. The growth plates in long bones and the sphenobasilar suture are temporary synchondroses.

1.3.2.3 Synostoses

Synostoses are osseous fusions of two adjacent bones. They evolve out of ossified syndesmoses or synchondroses.

1.3.2.4 Symphyses

Symphyses are (unlike synchondroses) permanent fusions between bones. They consist of a fibrocartilaginous tissue.

1.4 Anatomy of the skull and its sutures

1.4.1 The skeleton of the head

The skeleton of the head can be divided into different parts. The cranium is the bony structure of the head without the mandible and consists of the cerebral and facial skull, also named neurocranium and viscerocranium. They develop from separated embryological origins.

In general, the human skull is known to consist of twenty-eight bones, though there are some different sources that for example count paired bones as only one bone, exclude the ear ossicles or include the hyoid bone of the neck. (1,40)

The bony structure of the human skull functions mainly as a protection for the brain from injuries. It also ensures a stereoscopic vision by keeping a determined distance between the eyes and helps localizing the direction and distance of sounds by giving the hearing organs a fixed place.

1.4.1.1 The neurocranium

Eight bones, namely the occipital bone, the sphenoid, the ethmoid, the frontal bone, the two parietal and the two temporal bones, form the neurocranium.

The cerebral or brain skull can be divided into an upper section called the vault or skull cap (also calvaria cranii in latin) and a lower part called the skull base or basis cranii. The skull cap is formed by parietal bones and their adjacent parts of the frontal, temporal and occipital bones. The rest of the frontal, temporal, occipital and sphenoid bones form the skull base.

The neurocranium mainly forms the cranial cavity. It contains the brain and ensures its protection from a lot of different possible injuries.

1.4.1.2 The viscerocranium

The fourteen bones of the viscerocranium are the vomer, the mandible, two maxilla, two nasal bones, two nasal conchae, two palatine bones, two zygomatic bones and two lacrimal bones. The viscerocranium supports the face.

1.4.2 The joints of the skull

Apart from one bone, the mandible, all the skull bones are connected through sutures. They ossify at different ages and allow skull growth, though they are mainly immovable.

There are a few certain sutures with special names of their own but generally most sutures are named for the two bones they join.

1.4.2.1 List of sutures

Since most of the skull bones are paired, sutures occur often pairwise as the right and left side of a certain suture.

The frontal suture, also called metopic suture, is a single suture. It is located between the two frontal bones which usually fuse into a single bone. A persistent metopic suture is called metopism and can be found partially or fully ossified without any clinical significance, though a fracture should be rejected in trauma patients. (23,32,41,42)

The sagittal suture is a single suture found along the midline between the parietal bones. Its potential for age determination is discussed controversially. (20,43)

The paired lambdoid suture joins the parietal and occipital bones on the right and left side of the posterior skull. It is continuous with the paired occipitomastoid suture and in focus of contemporary and former age assessment. (6,16,36)

The occipitomastoid suture is a paired suture joining the occipital and temporal bones on the right and left side of the posterior inferior skull.

The sphenoccipital suture is also located in the skull base and joins as a single suture the occipital and sphenoid bone. The various ossification centres of the occipital bone lead to different studies that base on evaluating the sutures between the occipital bone and its neighbouring skull bones for age assessment. (44–48)

The sphenosquamous suture occurs as a paired suture between the left and right sphenoid bone and the squamous part of the temporal bone on each side.

These six different sutures listed above are the sutures I have measured and assessed for this study. I wanted to include single and paired sutures of the skull cap and skull base into the scoring system.

Further important sutures are for example the paired coronal suture which is between the frontal and parietal bones, the paired squamosal suture occurring the parietal and temporal bone and the left and right petrosquamous suture which join the two parts of the temporal bone on each skull side. The sphenofrontal suture, sphenoparietal suture, sphenozygomatic suture, sphenothmoidal suture and sphenopetrosal suture are sutures between the sphenoid

bone and its neighbouring skull bones. The remaining sutures join each cranial skull bone and its neighbouring bones and are for example the frontoethmoidal suture and the zygomaticofrontal suture.

1.4.3 Intra sutural bones

In some individuals, there are extra bones within a suture, which develop in addition to the usual regions of ossification of the cranium. These intra sutural bones are called wormian bones and are found most commonly in the lambdoid suture. Wormian bones can be used as diagnostic markers for several diseases, most importantly for primary detection of osteogenesis imperfecta. (1,19)

1.4.4 Histology of sutures

Various tissues are in focus of biological and anthropological research. The constantly developing of cranial bones and their sutures is one of the main reasons why these areas are a point of interest in scientific research. (18,49,50)

Between two cranial bones, the layer of the periosteum separates and builds an ectocranial and endocranial layer of connective tissue which is the anatomical boundary of a suture. The inner suture mainly consists of connective tissue based on fibrous and collagen fibres. Sharpey's fibres are bundles of collagen tissue bridging the suture gap between the skull bones and show ingrowth into the joint bones. Their distribution depends on separating forces, which leads to a numerous occurrence of Sharpey's fibres at areas of great forces of separation. Blood vessels and nerves follow the course of the Sharpey's fibres and enter the Haversian canals. (51,52)

1.4.5 Types of sutures

A suture's appearance depends on the affecting decisive force. The shape of the bony edges defines the following types of sutures.

A limbous suture, e.g. the squamous suture, performs as mitre joint. The articular surfaces of the joining bones are bevelled and the plane of the suture is sloping. When exposed to pressure or compression the sutural surfaces glide upon each other.

Serrate sutures show a large movement range and are found in areas of active growth. The sagittal suture is a serrate suture. (52)

Mixed forms of limbous and serrate sutures are e.g. the coronal suture and lambdoid suture where the bone edges are rather squared but still fit into each other.

Plane sutures, such as the internasal suture, work as simple buffers or butt joints where two

flat edges of the neighbouring bones run parallel to each other and can slide or spread in a limited extent.

The Schindylesis, e.g. the sphenomeral suture, is a form of suture where the surface of one bone fits into the crest of another and is therefore also called “wedge-and-groove” joint. (53)

The area where overlapping bone edges change their tendency from looking inward to the outside, or vice versa resp., is called key pivot point. These zones are important motion axes and allow extension and flexion of bones when the skull is exposed to different forces. (51,54)

1.4.6 The new-born skull structure

The ratio of head to body length and weight of a new-born is different from an adult. New-borns have a larger head but the viscerocranium is small, the neurocranium predominates. The ratio of viscerocranium to neurocranium of a new-born is 1:8 and develops to 1:2 at the age of an adult. (40,55)

The new-born skull counts 45 bones because they are not fully ossified and separated from each other. The available space between the bones is filled with cartilage and connective tissue. (1)

The sutures are still soft and wide-ranging because they had to permit slight motion of the skull bones during birth.

Fontanelles are six soft regions of the new-born skull where more than two bones come together. They occur as big gaps which consist usually of dense connective tissue at that moment of life. Along with the cartilaginous skull parts, the fontanelles' function is to ensure an overlap and motion during the process of through-passage of the head at birth. They usually close until the second year of life. (1,51)

1.4.7 Ossification of the skull bones and sutures

1.4.7.1 Desmal ossification

The “direct formation of bones through differentiation of mesenchymal progenitor cells in osteoblasts and subsequent production of bone” (56) is described as desmal ossification. In human skull, most of the vault and the facial bones develop via desmal ossification. (51,56)

1.4.7.2 Endochondral ossification

“During endochondral ossification, chondrocytes proliferate, undergo hypertrophy and die; (...) and osteoblasts (...) deposit bone on remnants of cartilage matrix.” (57) The skull base is mainly built through endochondral ossification.

1.4.7.3 Ossification of the sutures

The process of suture ossification is called synostosis and “occurs when small tongues of ossified tissue stretch across the sutural gap and link up slowly along the length of the suture until the union is complete” (8). (22)

There are general known ossification times of sutures which can be related to the age of a person, but various studies showed a physiological variability in the closure of sutures. Also, there is differences in radiological and histological definition of a closed suture (4,8,18,58–60).

The following list gives an overview of the ossification of the sutures I have measured and scored in this study.

The frontal suture closes usually between the first 3 to 9 months of life. The term metopic suture is especially used when the suture persists into old age. (61)

The beginning of the sagittal suture ossification is at the age of 22 years and the complete closure is at the age of about 35 years. The lambdoid suture starts to close at 26 years and shows ossification at the age of 47 years. (62,63)

The sutures of the skull base show a beginning of ossification in childhood. The sphenoccipital suture begins to close at the age of 6-13 years and is usually ossified between 13 – 17 years. (64)

The sphenosquamous suture shows beginning of ossification at 6 years, but the process “can take as long as 10 years”. (19)

Occipitomastoid suture normally closes in adolescence at 15 and 16 years of age. (19,65)

The term craniosynostosis is the diagnosis of premature closed sutures which can influence skull growth and lead to unusual skull shapes.(23,28–30,50,66,67)

1.4.8 Functions of sutures

As already outlined, the sutures’ function along with the fontanelles is to ensure motion and slight overlap of the skull bones during through-passage of the head at birth. In childhood and adolescents, the sutures allow growth of the skull at the same time as they and the intracranial dura mater prevent a separation of the skull bones. They allow minimal

motion of the skull and absorb vibrations and other mechanical forces that affect the skull. (51,64)

1.5 Skull imaging

For a better comprehension of using CT and MRI images in evaluation of the cranial sutures I want to give a short overview in indications and findings of these two cranial imaging methods.

1.5.1 CT findings of the skull

In trauma patients, which are the main included patients in this study, the reason for a cranial CT is to exclude injuries of the head, e.g. hemorrhages. Regarding the bony structure of the skull, suspected fractures, especially in the region of the skull base are a main indication for using CT as the imaging modality. The evaluation of pathologies in the skull is based on normal findings compared to aberrations, which have to be assessed in awareness of physiological variances. (19,33)

There are also variations of the skull related to different ages or developmental stages. For example the infant skull contains more hematopoietic bone marrow than an adult skull, which leads to a different appearance in the CT images. (68)

1.5.2 MRI findings of the skull

Main reason for using cranial MRI scanning in trauma patients is the sensitivity on the detection of brain injuries. The CT remains superior to MRI when it comes to detection of bone fractures, but the MRI is the preferred method for revealing pathologies in soft tissue structures. For some questions, the MRI can be as sensitively as CT imaging. (69)

2 MATERIAL & METHODS

2.1 Hypothesis and aims

The aim of this project was an analysis of cranial CT and MRI images regarding subjective and objective characteristics of the cranial sutures. Identifiable patterns of suture ossification in certain age groups would allow retrograde conclusions of age determination by cranial CT and MRI findings. These ambitions are meaningful in the field of forensics amongst others.

2.2 Study design

The following study was a retrospective single-center study performed at the Medical University of Graz.

The data query for the radiological images was requested at the medical data management of the Landeskrankenhaus Graz and the database research covered a time interval from November 2008 to June 2017 for CT and a time interval from January 2006 to February 2017 for MRI images.

In consideration of several exclusion criteria the study included CT images of 73 patients and MRI images of 26 patients.

The study protocol was approved by the ethical review committee of the Medical University of Graz (date 6th of July 2017, reference number: 29-528 ex 16/17).

2.3 Patients

For all patients, inclusion criteria were a cranial CT resp. MRI scan during the last 9 resp. 11 years. The patients were mainly trauma patients whose physical injuries usually don't interfere with the ossification grade of the cranial sutures and who are generally healthy otherwise.

Exclusion criteria were a premature suture closing, also called craniosynostosis, or other syndromal diseases that affect the skull. Scans of patients suffering from growth disorder or diseases related to a disturbance of growth, such as renal insufficiency, endocrinal syndromes (e.g. adreno-genital syndrome), disorders of sex chromosomes (e.g. Turner syndrome), and patients that underwent hormone treatment, chemotherapy or radiation treatment were excluded from the study.

For this retrospective study, six age groups were set. The age limits for each group were based on the international age categories of the *International Commission on Radiological*

Protection (ICRP). Group 1 included patients in their first year of life and was defined by a minimum age of 0 days and a maximum of 11 months. Group 2 included patients from 1 year of age to 4 years 11 months. Group 3 was defined by age from 5 years to 9 years 11 months. Group 4 included patients from 10 years to 13 years 11 months. The adolescents between 14 years and 17 years 11 months built group 5. From 18 to 99 years the adults were included into one group, group 6.

To fulfill data protection regulations in this study, all patients were defined by an ID which included neither name nor birth date nor other personal identification data.

2.3.1 CT patients

Total number of cases in CT assessment was n=73 (female 37%). The mean age of the patients in group 1 was 0 years \pm 0 (or 4 months respectively), the number of cases was n=2 (female 50%). The mean age in group 2 was 3 \pm 2 years and the group 2 consisted of n=2 (female 0%) as well. Group 3 showed a mean age of 7 \pm 1 years with n=7 (female 14%). Group 4 included n=19 study patients (female 37%), the mean age was 12 \pm 0 years. The n=19 adolescents (female 32%) in group 5 showed a mean age of 16 \pm 0 years. The adults were included in group 6 with an amount of n=24 (female 50%) and a mean age of 53 \pm 4 years.

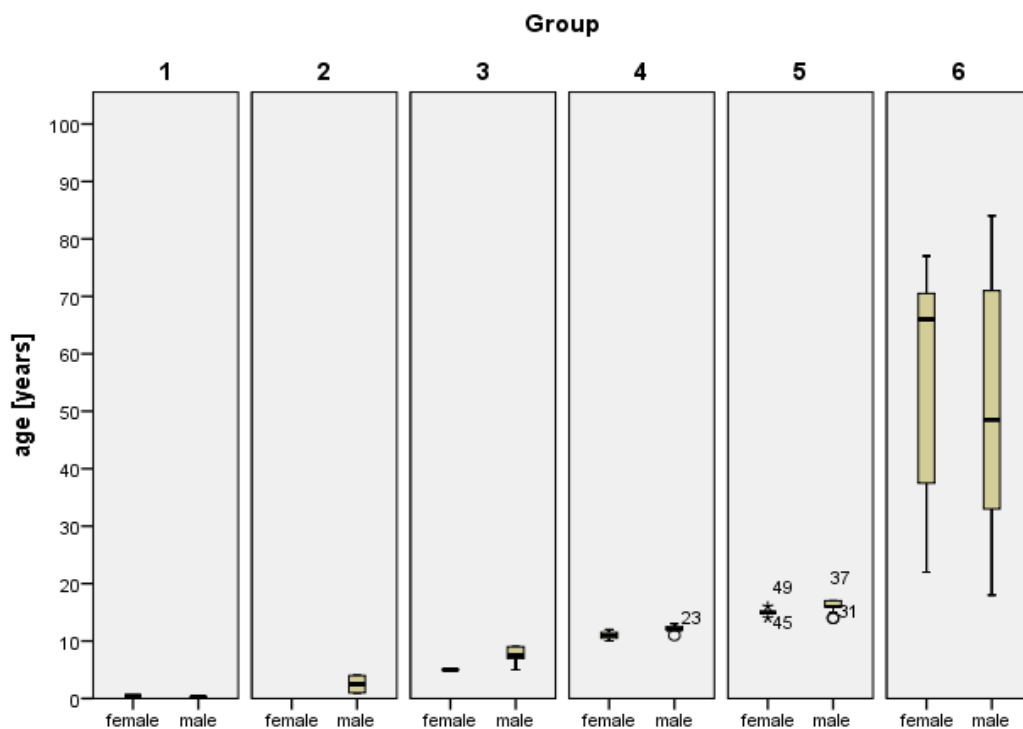


Figure 1 Boxplot showing age of male and female CT patients for each group.

2.3.2 MRI patients

Total number of cases in MRI assessment was $n=26$ (female 50%). There were no study patients that fit criteria for group 1.

Group 2 included 2 study patients (female 100%), mean age was 3 ± 1 years. Age of both study patients (female 50%) in group 3 was 5 years (mean 5 ± 0). Mean age of the 3 study patients (female 0%) in group 4 was 11 ± 1 years. Group 5 included 6 patients (female 67%), mean age was 17 ± 0 . Group 6 showed a mean age of 49 ± 4 years, it consisted of 13 patients (female 46%).

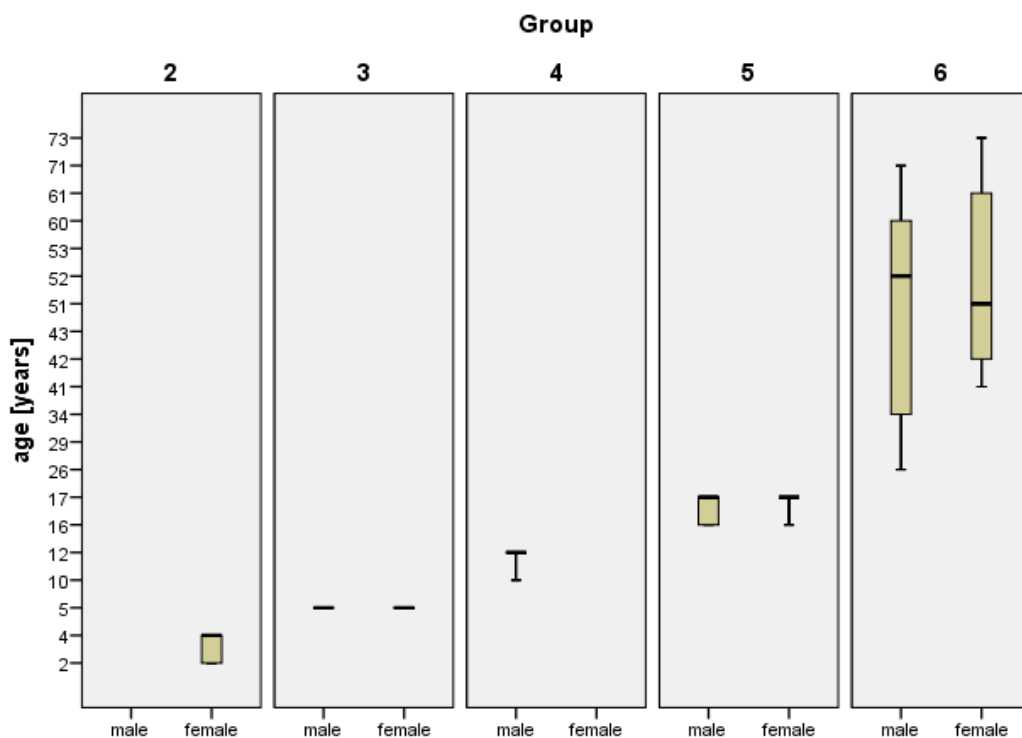


Figure 2 Boxplot showing age of male and female MRI patients for each group.

2.4 CT and MRI data

For this retrospective study data query for CT and MRI images was requested from medical data management at the LKH-Univ. Klinikum Graz.

Data of patients who met exclusion criteria was diminished.

For CT data only images with a slice thickness of 1,50 mm was used.

All MRI images were in Flash-3D-sequence with a slice thickness of 1 mm.

2.5 Viewer and editing programs

To view CT and MRI images and to measure the sutures of the skull the OsiriX Lite free Version 8.5.2 was used.

To save measurements the values were transferred and saved in MicrosoftExcel (version

15.32) spreadsheets.

Statistic tests, tables and figures were assessed using IBM SPSS Statistics 23 (German language version).

2.6 Sutures

For measuring and scoring 6 different sutures were selected. The selected sutures of skull cap were the metopic suture, the sagittal suture and the lambdoid suture (Figure 3, Figure 7). The sutures of skull base were the sphenoccipital suture, the sphenosquamous suture and the occipitomastoid suture (Figure 4, Figure 5, Figure 6, Figure 8, Figure 9). The left and right side of the paired sutures were measured and scored separately as one single suture.

2.7 Scoring

The general scoring method was to give ossification score points for each measurement: 1 point for an open suture area, 2 points for a closing area and 3 points for an ossified suture area. All measurements of a suture were taken in the area where the certain suture is usually found.

2.7.1 Suture score

Each suture was divided into 3 parts: an anterior, middle and posterior part (or depending on the anatomical course: a superior, middle and inferior part resp.). Three measurements were taken in each third of the suture which lead to 9 measuring points for each suture.

An open suture was defined as a suture with 9 open measuring points and scored therefore 9 points. An ossified suture scored 27 points. Suture score of 10-26 points was found in closing sutures. The suture score points were summed up and created the skull cap score, the skull base score and the total score.

2.7.2 Skull cap score

Score of skull cap was created by adding up score points of the metopic suture, the sagittal suture and the right and left lambdoid suture. The skull cap score showed a minimum of 36 score points, which defined an open skull cap and a maximum of 108 score points, which defined an ossified skull cap. Skull cap score of 37-107 points was found in closing skull caps.

2.7.3 Skull base score

The sum of suture scores of the sphenoccipital suture, the left and right sphenosquamous

suture and the left and right occipitomastoid suture created the skull base score. 45 skull base score points defined an open skull base and 135 points defined an ossified skull base. Closing skull bases showed score points between 46-134.

2.7.4 Total score

Total score of one skull was created by summing up all suture score points of one skull. An open skull scored 81 points and an ossified skull scored 243 points. Score points of 82-242 were defined as closing skulls.

2.7.5 CT aspects

Sutures of the skull base were measured and scored in axial view. If possible then metopic, sagittal and lambdoid sutures were measured and scored in coronal view. If no different views were available, then these measurements were also taken in axial view. The minimum distance between two measuring areas was defined as 1 mm to ensure a better distribution of measuring points among the course of the suture.

2.7.5.1 Objective evaluation score in CT images

In CT images, the objective evaluation score (OES) was defined by Hounsfield-units (HU). Three length measurements were taken per suture section (= 9 per suture) using the line tool of OsiriX Lite. In an open suture area, the lowest HU was <250 and scored 1 point. Closing areas showed lowest HU between 250 and 500 HU and scored 2 points. Ossified areas showed HU > 500. Optimal HU limits were set after my own evaluation by measuring cortical bone which showed HU > 500 and weak/ soft tissues which showed HU < 250.

2.7.5.2 Suture width determination

The minimum distance between the two skull bones was saved as the width of the suture in mm at each measuring area. Length measurement tool was used to determine the suture width in mm, which was defined as the length of the section HU <500 between two compact bone tissues of HU > 500. If there was no measurable HU < 500 then the suture width was defined as 0 mm at this point.

2.7.5.3 Subjective evaluation score in CT images

The window-width/window-level (WW/WL) was manually adjusted to 375 WL/ 250 WW to evaluate the further subjective evaluation score (SES). A visible black gap between two

skull bones at the measuring point implied an open suture point and scored 1 SES point. Visible opacity at the gap point was defined as closing suture point and scored 2 SES points. No visible gap, resp. a total white measurement point implied an ossified suture point and scored 3 SES points (Figure 4, Figure 5, Figure 6).

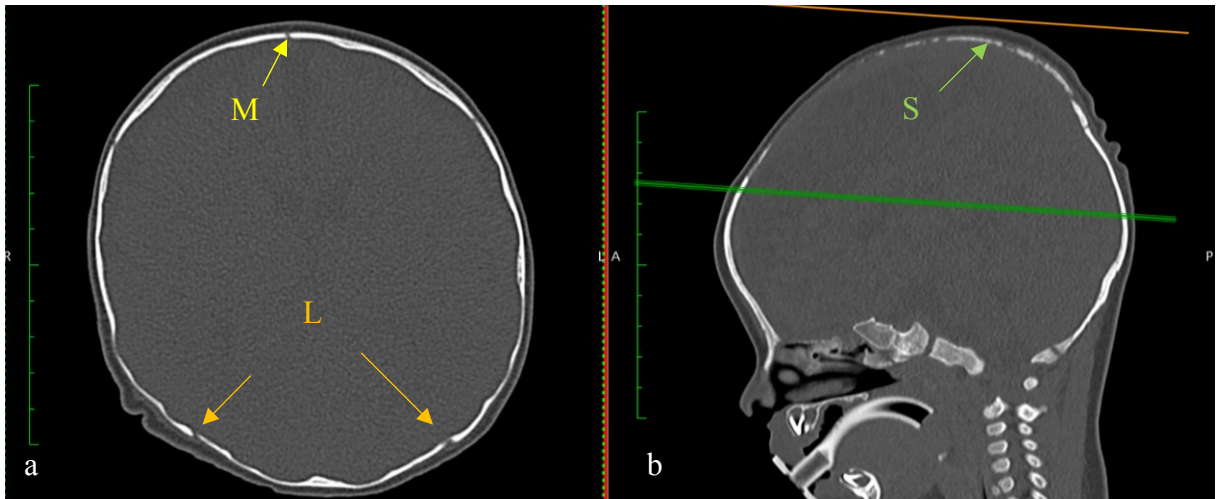


Figure 3 CT image of a pediatric skull of a 3 months old male in bone window showing assessed sutures of the skull cap in, a axial view and b sagittal reformat (yellow arrow: metopic suture, orange arrows: left and right lambdoid suture, green arrow: sagittal suture).

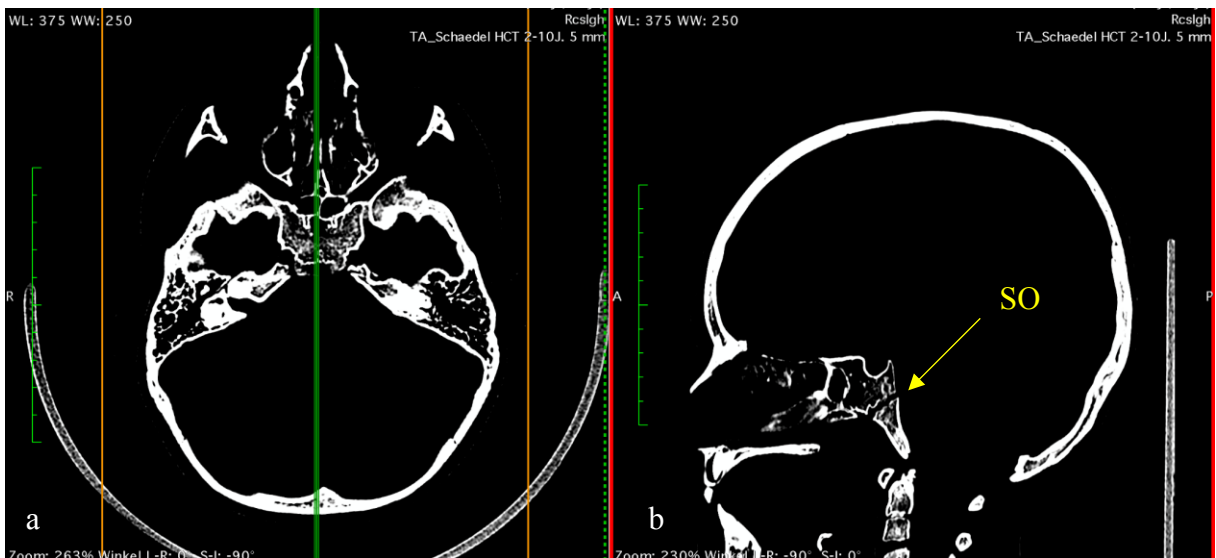


Figure 4 CT image of a pediatric skull of a 4 years old male in manual WW/WL setting in a axial view and b sagittal reformat (yellow arrow: sphenooipital suture).

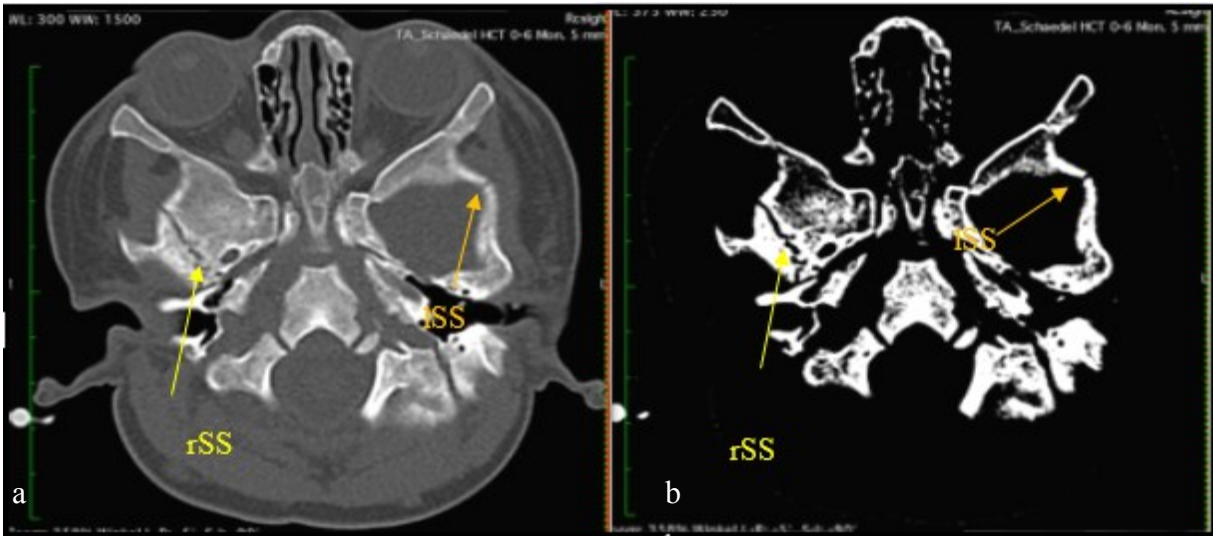


Figure 5 CT image of a pediatric skull of a 3 months old male in axial view in a bone window and b manual WW/WL settings (yellow arrow: middle and posterior part of right sphenosquamous suture, orange arrow: anterior part of left sphenosquamous suture).

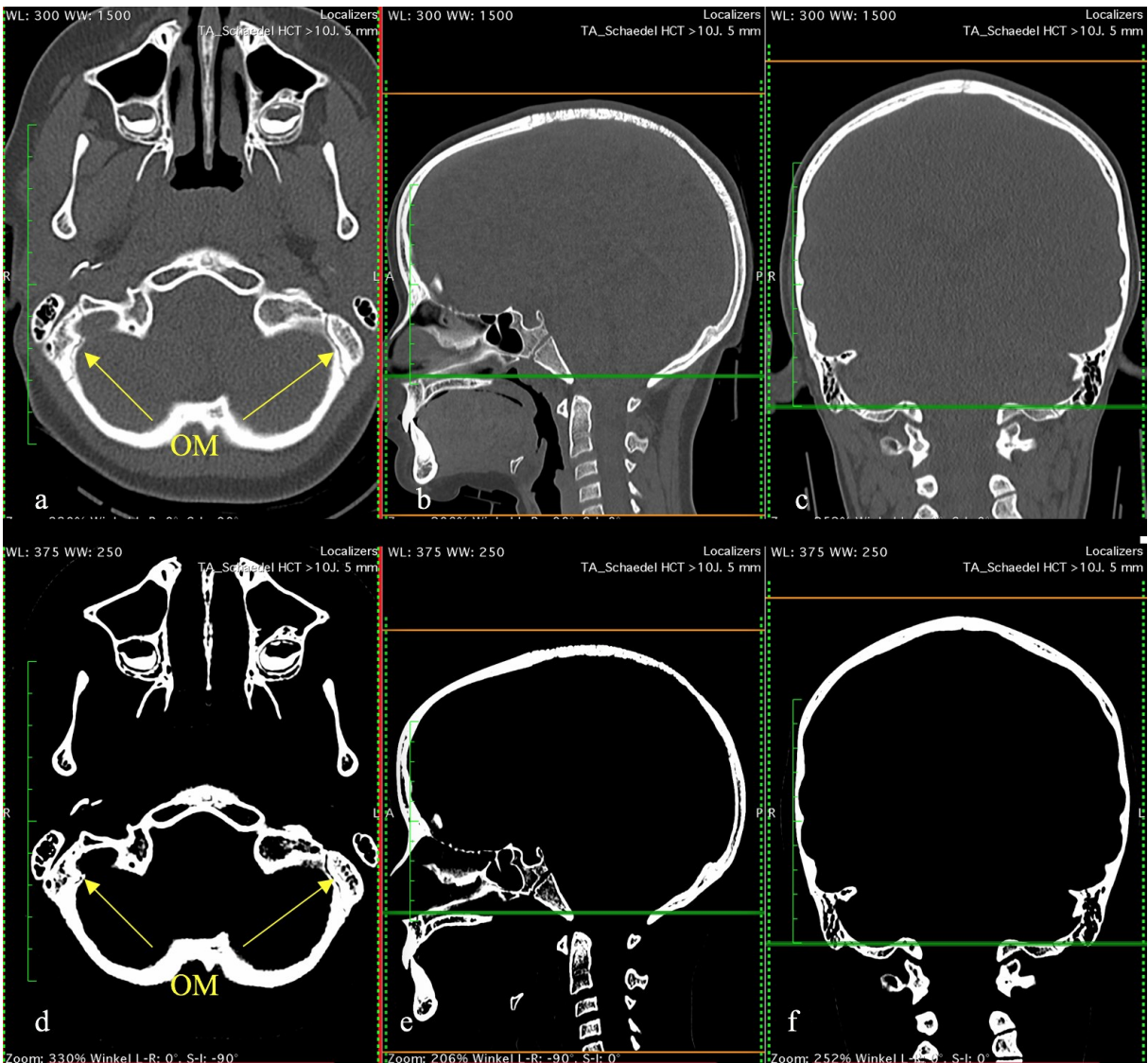


Figure 6 CT image of a skull of a 10 years old female in a-c bone window and d-f manual WW/WL settings in a d axial view, b e sagittal and c f coronal reformat (yellow arrows: left and right occipitomastoid suture).

2.7.6 MRI aspects

Sutures were measured in the available axial or sagittal view. Due to lower contrast than in CT images, area measurements instead of length measurements were taken, using the area tool of OsiriX Lite. In MRI images, 3 area measurements per section were taken. The measurement area was smaller than 1mm^2 to not include neighboring structures. Mean value of signal intensity of each measuring area was taken for further scoring.

2.7.6.1 Objective evaluation score in MRI images

In MRI OES an open suture was defined as a mean signal intensity value of at least 300 in a measuring area and scored 1 point. 2 points scored closing areas, where mean signal intensity was between 100 and 300. Ossified areas showed mean signal intensity <100 and scored 3 points. Optimal signal intensity limiting values were set after my own evaluation by measuring reference values of soft tissue (e.g. fat) with a minimum signal intensity of 300 and cortical bone with a maximum signal intensity of <100 .

2.7.6.2 Subjective evaluation score in MRI images

For MRI SES, the measuring areas were evaluated in comparison to their neighboring tissues. A visible hyper intense area in comparison to medullary bone was scored with 1 point as an open suture area. 2 points scored closing suture areas which showed and isointense signal intensity in comparison to medullary bone. An ossified area was defined as hypo intense area or lack of signal in comparison to medullary bone and scored 3 points.

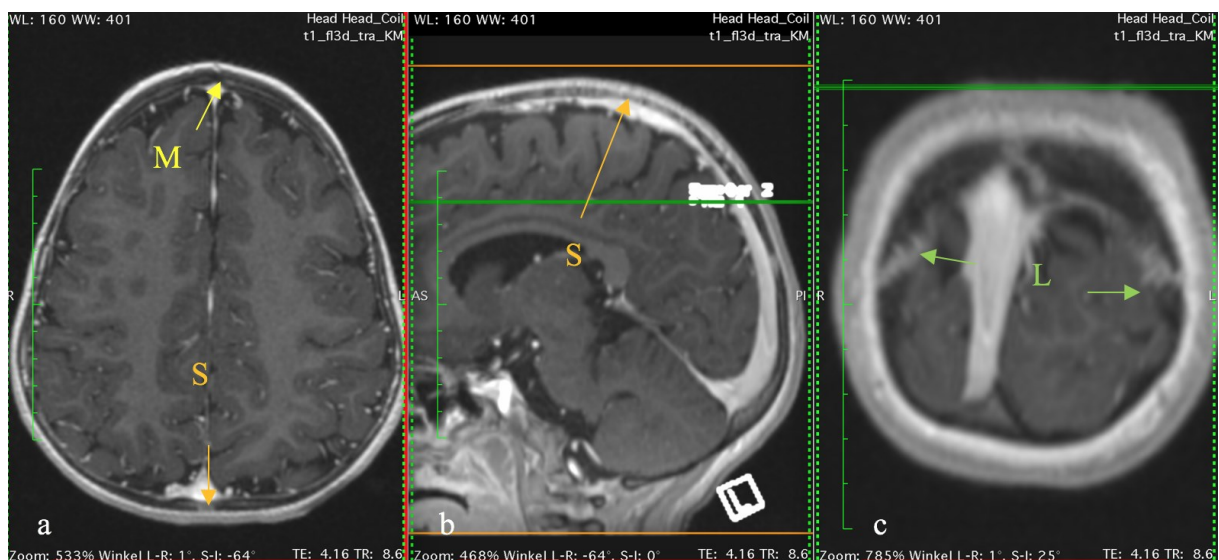


Figure 7 MRI of a pediatric skull of a 4 years old female showing assessed sutures of the skull cap in **a** axial view, **b** sagittal and **c** coronal reformat (yellow arrow: metopic suture, orange arrows: sagittal suture, green arrows: left and right lambdoid suture).

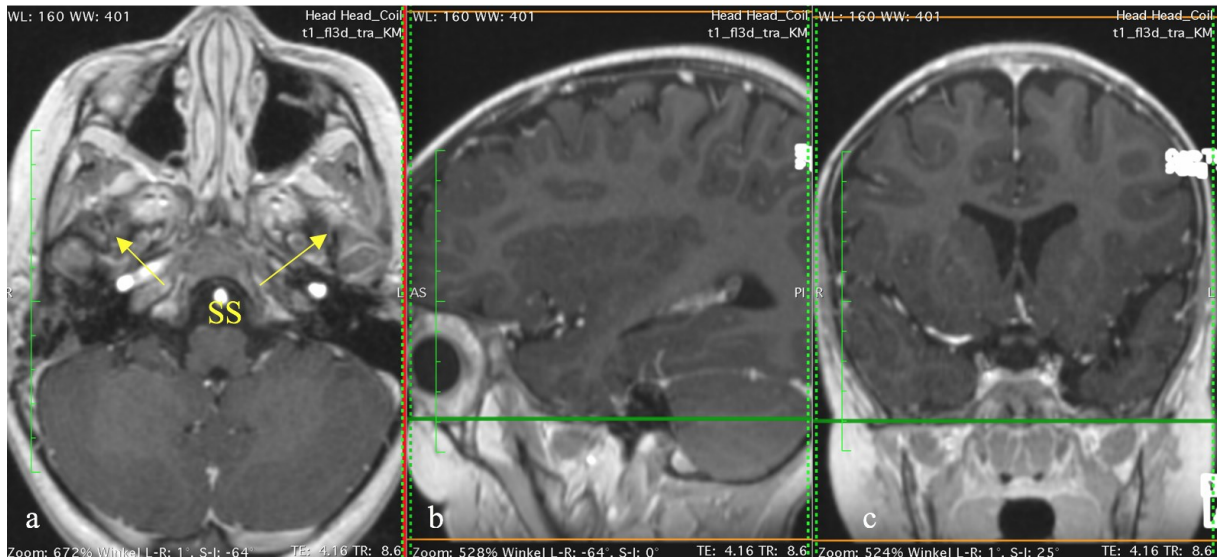


Figure 8 MRI of a pediatric skull of a 4 years old female showing the sphenosquamous sutures (yellow arrows) in a axial view, b sagittal (right sphenosquamous suture) and coronal reformat.

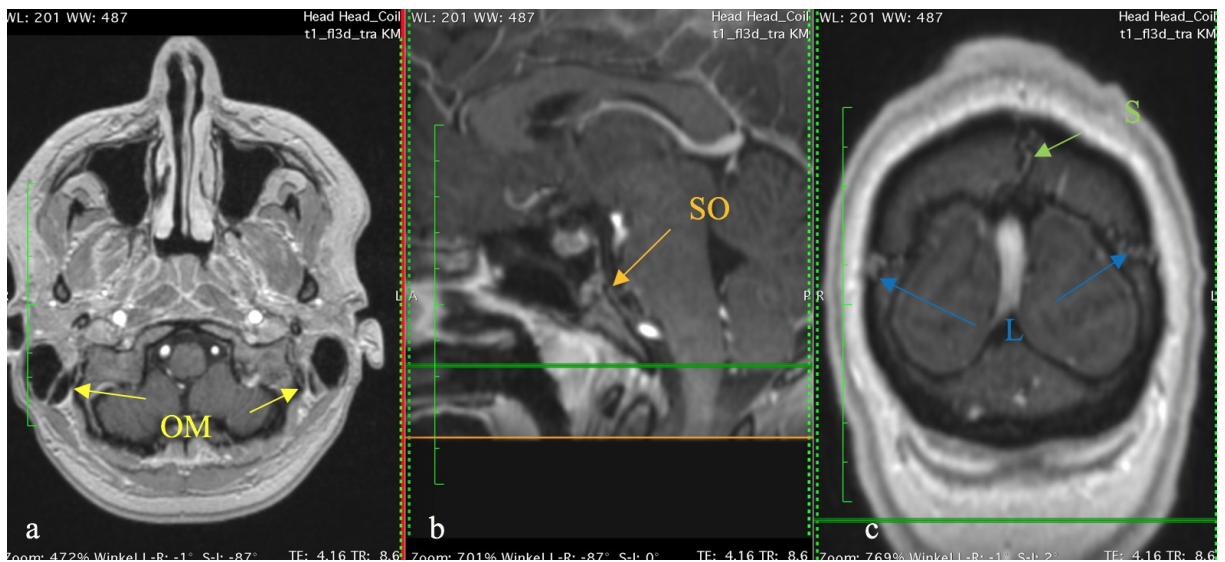


Figure 9 Cranial MRI of a 16 years old male in a axial view, b sagittal and c coronal reformat (yellow arrows: left and right occipitomastoid suture, orange arrow: sphenoccipital suture, green arrow: sagittal suture, blue arrows: left and right lambdoid suture).

2.8 Statistics

Descriptive and explorative statistics included line and bar graphs, boxplots and histograms to view the distribution of the ossification score data across the study population by group. Certain figures showed data separated by sex to reveal gender aspects. Numbers were declared without the use of decimals. Means are described as value \pm SE. The significance level for all tests was 0,05.

To evaluate a significant difference between the objective and subjective scoring method, related means of total OES and total SES were compared. The difference between skull cap OES and skull cap SES was also analyzed, as well as the difference between skull base OES and skull base SES. Due to small number of cases n (CT n=73, MRI n=26) the Wilcoxon-test was applied to compare total OES to total SES, skull cap OES to skull cap SES and skull base OES to skull base SES.

OES data was analyzed by analysis of variance to compare means of total OES, means of skull cap OES, means of skull base OES and means of suture OES by group. An ANOVA and Bonferroni post hoc test were applied to relate adjusted means of the score and to determine significant variations between the groups.

Differences in suture ossification between adults aged 18 to 99 years (group 6) and adolescents aged 14 to <18 years (group 5) were analyzed by using the results of the ANOVA and Bonferroni post hoc tests. OES points of group 5 and group 6 were compared in mean of total OES, mean of skull cap OES, mean of skull base OES and mean of suture OES.

Differences between left and right side of paired sutures (the lambdoid suture, the sphenosquamous suture and the occipitomastoid suture) were analyzed by using the Wilcoxon test.

Gender aspects were analyzed by using Mann-Whitney-test to evaluate a difference in total OES, skull cap OES and skull base OES.

3 RESULTS

3.1 Measurement and scoring

The established scores for CT and MRI measurements were based on 81 measurements per skull and were the basis for the statistical calculations. (Table 27, Table 28)

3.2 CT results

3.2.1 OES vs SES

To evaluate a significant difference between the objective and subjective scoring method, related means of total OES and total SES were compared. The difference between skull cap OES and skull cap SES was also analyzed, as well as the difference between skull base OES and skull base SES.

Wilcoxon test showed a significant difference ($p=0$) between mean of total objective evaluation score points and mean of total subjective evaluation score points (Table 2, Table 3).

The lowest value of total OES of all patients was 81 points, the highest measured value was 243 points. The mean value of total OES points of all patients was 200 ± 4 (Table 1).

The lowest value of total SES of all patients was 81, the highest measured value was 241 points. The mean value of total SES points of all patients was 203 ± 4 .

The different means of total OES and total SES of each group were illustrated in Figure 10 and Figure 11.

Wilcoxon tests also showed a significant difference ($p=0$) between OES and SES in means of skull cap score and between OES and SES in means of skull base score (Table 2, Table 3).

Descriptive statistic results showing mean values of total OES, total SES, skull cap OES, skull cap SES, skull base OES and skull base SES of CT patients were listed in Table 1.

Wilcoxon test results of comparing total OES to total SES, skull cap OES to skull cap SES and skull base OES to skull base SES were shown in Table 2. The statistical significance of the test results was listed in Table 3.

An illustration of the mean values of total OES and mean values of total SES per group was given in a scatterplot in Figure 10 and in a line graph in Figure 11.

Due to these results and due to better reproducibility of objective evaluations the OES points were used for further testing.

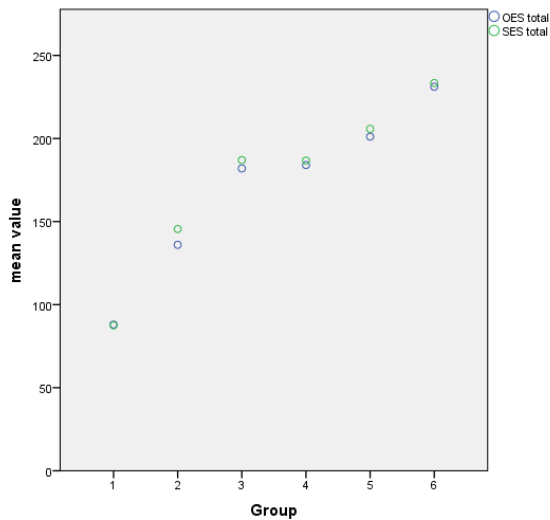


Figure 10 Scatterplot showing mean value of total OES and mean value of total SES points of CT patients of each group.

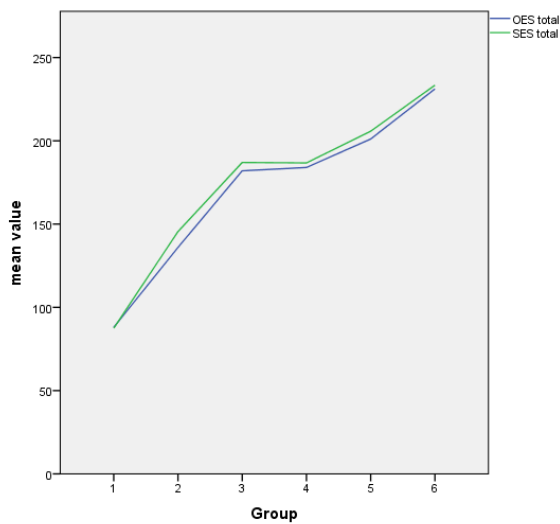


Figure 11 Line graph showing mean value of total OES and mean value of total SES points of CT patients of each group.

	OES total	SES total	OES skull cap	SES skull cap	OES skull base	SES skull base
Mittelwert	199,82	203,22	98,10	99,62	101,73	103,60
N	73	73	73	73	73	73
Standardabweichung	31,934	31,448	12,817	12,414	22,552	22,122
Standardfehler des Mittelwertes	3,738	3,681	1,500	1,453	2,640	2,589

Table 1 Descriptive statistic results showing mean values of total OES, total SES, skull cap OES, skull cap SES, skull base OES and skull base SES of CT patient (German designations).

	N	Mittlerer Rang	Rangsumme
SES total - OES total	Negative Ränge	5a	21,00
	Positive Ränge	64b	36,09
	Bindungen	4c	
	Gesamt	73	
SES skull cap - OES skull cap	Negative Ränge	3d	13,33
	Positive Ränge	46e	25,76
	Bindungen	24f	
	Gesamt	73	
SES skull base - OES skull base	Negative Ränge	7g	19,86
	Positive Ränge	57h	34,05
	Bindungen	9i	
	Gesamt	73	

a. SES total < OES total b. SES total > OES total c. SES total = OES total d. SES skull cap < OES skull cap e. SES skull cap > OES skull cap f. SES skull cap = OES skull cap g. SES skull base < OES skull base h. SES skull base > OES skull base i. SES skull base = OES skull base

Table 2 Wilcoxon test results of comparing total OES to total SES, skull cap OES to skull cap SES and skull base OES to skull base SES (German designations).

	SES total - OES total	SES skull cap - OES skull cap	SES skull base - OES skull base
Z	-6,616b	-5,743b	-6,077b
Asymptotische Signifikanz (2-seitig)	,000	,000	,000
Exakte Signifikanz (2-seitig)	,000	,000	,000
Exakte Signifikanz (1-seitig)	,000	,000	,000
Punkt-Wahrscheinlichkeit	,000	,000	,000

b. Basiert auf negativen Rängen.

Table 3 Statistic results for Table 2 showing the statistical significance (German designations).

3.2.2 Group vs Group

3.2.2.1 Total OES, skull cap OES and skull base in a group by group comparison

Descriptive statistic results showing mean values of total OES, skull cap OES and skull base OES of CT patients were listed in Table 8.

Univariate ANOVA results of total OES, skull cap OES and skull base OES were shown in Table 4. The Bonferroni Post-Hoc test results comparing means of total OES, means of skull cap OES and means of skull base OES by group were shown in Table 5.

An illustration of total OES points per group separated by gender was given in the boxplot graph in Figure 12, of skull cap OES points in the boxplot in Figure 13 and of skull base OES points in the boxplot in Figure 14.

3.2.2.1.1 Total OES in a group by group comparison

The mean total OES in group 1 was 88 ± 7 and was the significant lowest compared to groups 2-6 ($p=0,002$ compared to group 2 and $p=0$ compared to group 3-6). Total OES of group 2 showed a mean value of 136 ± 13 and was also significant different to the other groups ($p=0,002$ compared to group 1 and $p=0$ compared to group 3-6). The two groups of adolescents and adults, group 5 and 6, showed the highest values of score points with a mean of 201 ± 4 in group 5 and 231 ± 1 in group 6, which were both significant different to each other and all the other groups ($p=0,09$ in group 5 to group 3 comparison, $p=0,01$ in group 5 to group 4 comparison, $p=0$ in the other comparisons as shown in Table 5).

With a mean value of 182 ± 3 group 3 showed a significant difference to groups 1,2,5 and 6 ($p=0,09$ compared to group 5, $p=0$ compared to groups 1,2 and 6). Group 4 showed a mean total OES of 184 ± 3 and was significant different to groups 1,2,5 and 6 ($p=0,01$ compared to group 5, $p=0$ compared to groups 1,2 and 6). In comparison to each other, group 3 and 4 showed no significant difference in means of total OES ($p=1$).

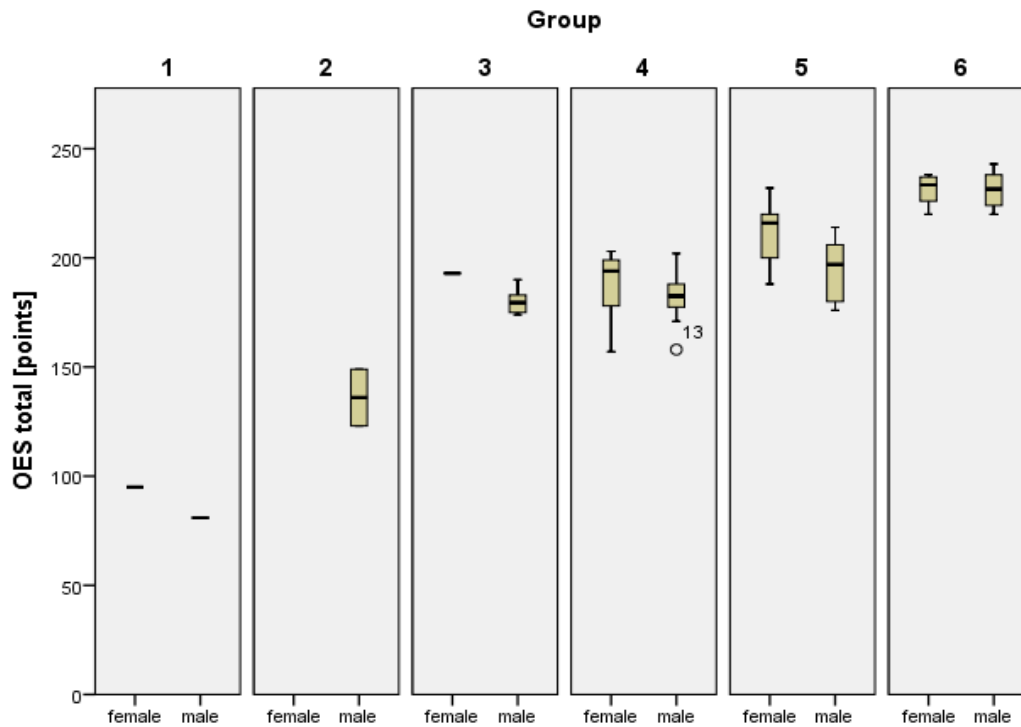


Figure 12 Boxplot showing total OES points of male and female CT patients of each group.

3.2.2.1.2 Skull cap OES in a group by group comparison

The means of OES of skull cap showed a significant difference in group 1 (43 ± 7) compared to the other groups and group 2 (66 ± 10) compared to the other groups ($p=0,08$ in group 1 to group 2 comparison, $p=0$ in the other comparisons as shown in Table 5). Group 3 (97 ± 2), 4 (99 ± 2), 5 (98 ± 2) showed no significant difference in comparison to each other ($p=1$ in comparisons group 3 to groups 4 and 5 and group 4 to group 5). Mean skull cap OES of group 6 (105 ± 1) was significant different to mean skull cap OES of group 5 ($p=0,013$).

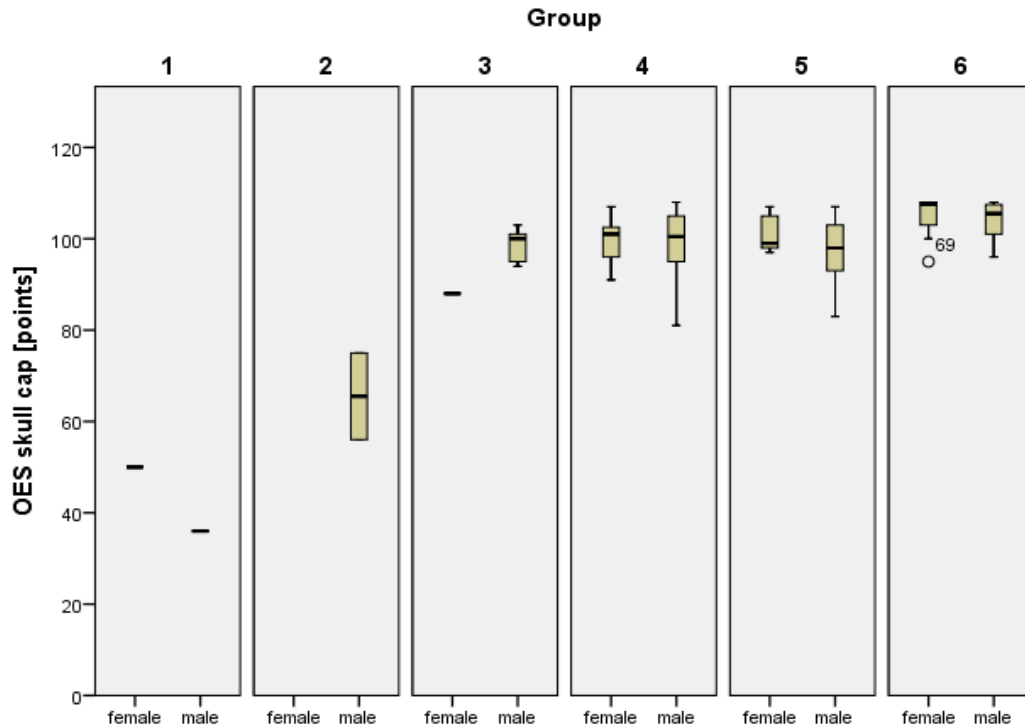


Figure 13 Boxplot showing skull cap OES points of male and female CT patients of each group.

3.2.2.1.3 Skull base OES in a group by group comparison

Skull base OES means showed a significant difference ($p=0$) in group 1 (45 ± 0) compared to group 3 (85 ± 4), 4 (85 ± 2), 5 (103 ± 3), and 6 (126 ± 1). Mean skull base OES of group 2 (71 ± 4) was significant different to means of group 5 and 6 ($p=0$). Group 3 was also significant different to group 5 and 6 ($p=0,001$ compared to group 5 and $p=0$ compared to group 6). Group 4, 5 and 6 were significant different to each other ($p=0$).

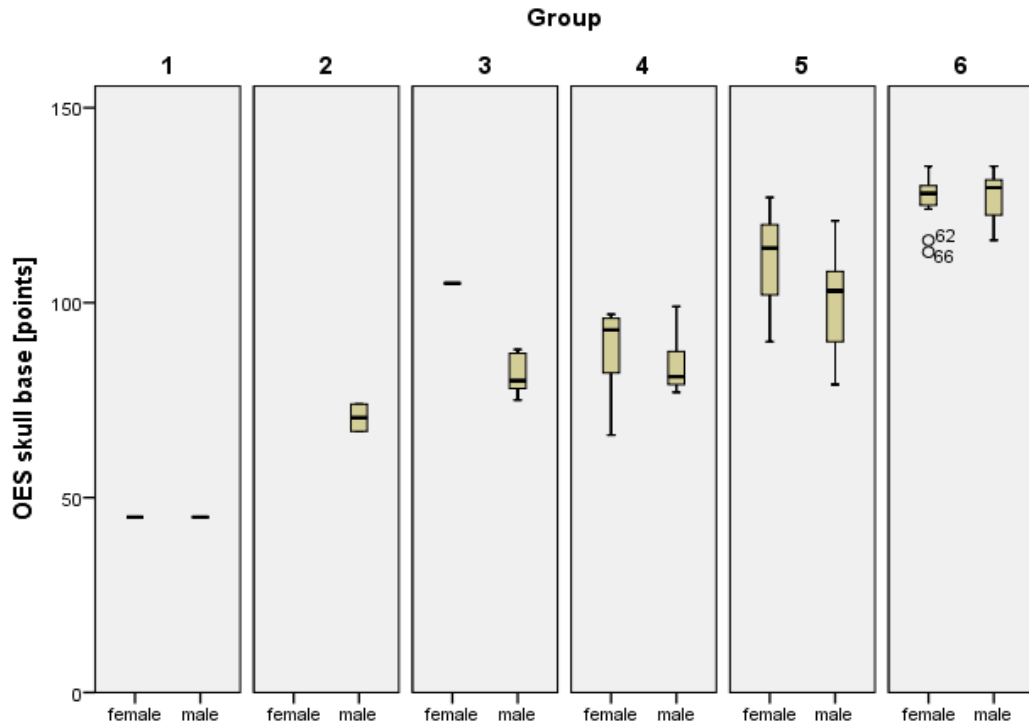


Figure 14 Boxplot showing skull base OES points of male and female CT patients of each group.

			Quadratsumme	df	Mittel der Quadrate	F	Signifikanz
OES total	Zwischen Gruppen	den	63745,562	5	12749,112	88,251	,000
	Innerhalb Gruppen	der	9679,123	67	144,465		
	Gesamt		73424,685	72			
OES skull cap	Zwischen Gruppen	den	9284,848	5	1856,970	48,916	,000
	Innerhalb Gruppen	der	2543,481	67	37,962		
	Gesamt		11828,329	72			
OES skull base	Zwischen Gruppen	den	30487,285	5	6097,457	66,631	,000
	Innerhalb Gruppen	der	6131,236	67	91,511		
	Gesamt		36618,521	72			

Table 4 Univariate ANOVA results for total OES, skull cap OES and skull base OES (German designations).

Abhängige Variable	(I) Group	(J) Group	Mittlere Differenz (I-J)	Standardfehler	Signifikanz
OES total	1	2	-48,000*	12,019	,002
		3	-94,000*	9,637	,000
		4	-96,000*	8,935	,000
		5	-113,105*	8,935	,000
		6	-143,167*	8,846	,000
		2	1	48,000*	12,019
	3	-46,000*	9,637	,000	
	4	48,000*	8,935	,000	
	5	-65,105*	8,935	,000	
	6	-95,167*	8,846	,000	
	3	1	94,000*	9,637	,000
	2	46,000*	9,637	,000	
	4	-2,000	5,314	1,000	
	5	-19,105*	5,314	,009	
	6	49,167*	5,163	,000	
	4	1	96,000*	8,935	,000
	2	48,000*	8,935	,000	
	3	2,000	5,314	1,000	
	5	-17,105*	3,900	,001	
	6	47,167*	3,691	,000	
	5	1	113,105*	8,935	,000
	2	65,105*	8,935	,000	
	3	19,105*	5,314	,009	
	4	17,105*	3,900	,001	
6	-30,061*	3,691	,000		
6	1	143,167*	8,846	,000	
2	95,167*	8,846	,000		
3	49,167*	5,163	,000		
4	47,167*	3,691	,000		
5	30,061*	3,691	,000		
OES skull cap	1	2	-22,500*	6,161	,008
		3	-54,286*	4,940	,000
		4	-56,158*	4,580	,000
		5	-55,158*	4,580	,000
		6	-61,750*	4,535	,000
		2	1	22,500*	6,161
	3	-31,786*	4,940	,000	
	4	-33,658*	4,580	,000	
	5	-32,658*	4,580	,000	
	6	-39,250*	4,535	,000	
	3	1	54,286*	4,940	,000
	2	31,786*	4,940	,000	
	4	-1,872	2,724	1,000	
	5	-,872	2,724	1,000	
	6	-7,464	2,647	,095	
	4	1	56,158*	4,580	,000
	2	33,658*	4,580	,000	
	3	1,872	2,724	1,000	
	5	1,000	1,999	1,000	
	6	-5,592	1,892	,065	
	5	1	55,158*	4,580	,000
	2	32,658*	4,580	,000	
	3	,872	2,724	1,000	
	4	-1,000	1,999	1,000	
6	-6,592*	1,892	,013		
6	1	61,750*	4,535	,000	
2	39,250*	4,535	,000		
3	7,464	2,647	,095		
4	5,592	1,892	,065		
5	6,592*	1,892	,013		
OES skull base	1	2	-25,500	9,566	,144
		3	-39,714*	7,670	,000
		4	-39,842*	7,111	,000
		5	-57,947*	7,111	,000
		6	-81,417*	7,040	,000
		2	1	25,500	9,566
	3	-14,214	7,670	1,000	
	4	-14,342	7,111	,716	
	5	-32,447*	7,111	,000	
	6	-55,917*	7,040	,000	
	3	1	39,714*	7,670	,000
	2	14,214	7,670	1,000	
	4	-,128	4,230	1,000	
	5	-18,233*	4,230	,001	
	6	-41,702*	4,109	,000	
	4	1	39,842*	7,111	,000
2	14,342	7,111	,716		

	3	,128	4,230	,000
	5	-18,105*	3,104	,000
	6	-41,575*	2,938	,000
5	1	57,947*	7,111	,000
	2	32,447*	7,111	,000
	3	18,233*	4,230	,001
	4	18,105*	3,104	,000
	6	-23,469*	2,938	,000
6	1	81,417*	7,040	,000
	2	55,917*	7,040	,000
	3	41,702*	4,109	,000
	4	41,575*	2,938	,000
	5	23,469*	2,938	,000

*. Die Differenz der Mittelwerte ist auf dem Niveau 0.05 signifikant.

Table 5 Bonferroni Post-Hoc-test results for group-by-group comparison of total OES, skull cap OES and skull base OES (German designations).

3.2.2.2 Suture OES in a group by group comparison

The group-by-group comparison of suture score means of each suture showed some significant results.

Descriptive statistic results showing mean values of the suture OES of each suture of CT patients were listed in Table 8.

Univariate ANOVA results of suture scores were shown in Table 6. The Bonferroni Post-Hoc test results comparing means of suture OES by group were shown in Table 7.

An illustration of mean values of suture OES points per group was given in the line graph in Figure 15.

3.2.2.2.1 Metopic suture OES in a group by group comparison

Mean metopic suture score of 16 ± 7 in group 1 was the significant lowest ($p=0$) compared to group 2 (27 ± 1), group 3 (27 ± 0), group 4 (27 ± 0), group 5 (27 ± 0) and group 6 (27 ± 0). Other group-by-group comparisons showed no significant difference ($p=1$).

3.2.2.2.2 Sagittal suture OES in a group by group comparison

Means of sagittal suture OES showed no significant difference ($p=1$) between the 2 youngest age groups, group 1 (9 ± 0) and group 2 (11 ± 1). There were significant differences between group 1 and group 3 (21 ± 2), 4 (23 ± 1), 5 (23 ± 1) and 6 (27 ± 0) as well as between group 2 and group 3, 4, 5 and 6 ($p=0,001$ in group 2 to 3 comparison, $p=0$ in the other comparisons as shown in Table 7). Group 3, 4 and 5 showed no significant difference to each other but to group 6 ($p=0,001$ in group 3 to 6 comparison, $p=0,008$ in group 4 to 6 comparison, $p=0,017$ in group 5 to 6 comparison).

3.2.2.2.3 Right lambdoid suture OES in a group by group comparison

Right lambdoid suture OES means showed difference between group 1 (9 ± 0) and group 3

(24 ±1), 4 (24 ±1), 5 (23 ±1) and 6 (26 ±0) (p=0), as well as between group 2 (15 ±4) and the older groups (p=0,001 in group 2 to 3 comparison, p=0 in group 2 to groups 4,5 and 6 comparisons). No other comparisons showed significant difference, except for group 5 compared to group 6 (p=0,03).

3.2.2.2.4 Left lambdoid suture OES in a group by group comparison

Means of OES of left lambdoid suture showed a significant difference between group 1 (9 ±0) and group 3 (26 ±0), 4 (25 ±1), 5 (25 ±1) and 6 (25 ±1), as well as between 2 (14 ±5) and the older groups (p=0). No other group-by-group comparisons reached significance (p=1).

3.2.2.2.5 Sphenooccipital suture OES in a group by group comparison

Means of OES of sphenooccipital suture showed a difference comparing group 5 (24 ±1) to group 1 (9 ±0), 2 (9 ±0), 3 (9 ±0) and 4 (11 ±0), as well as comparing group 6 (27 ±0) to group 1, 2, 3 and 4 (p=0). No other group-by-group comparisons showed significance (p=0,124 in group 6 to 5 comparison, p=1 in other comparisons as shown in Table 7).

3.2.2.2.6 Right sphenosquamous suture OES in a group by group comparison

Means of OES of right sphenosquamous suture showed a significant difference between group 1 (9 ±0) and group 2 (17 ±2) and to all the older groups (p=0,019 in group 1 to group 2 comparison, p=0,036 in group 2 to 3 comparison, p=0,004 in group 2 to 4 comparison, p=0 in comparison group 1 to groups 3-6 and group 2 to groups 5 and 6). Group 6 (26 ±0) showed a significant difference to group 3 (22 ±1) (p=0,001) and group 4 (23 ±1) (p=0) as well, but not to group 5 (25 ±1) (p=0,357).

3.2.2.2.7 Left sphenosquamous suture OES in a group by group comparison

Means of left sphenosquamous suture showed significant results in comparing means of group 1 (9 ±0) and group 2 (16 ±0) to each other and all the older groups (p=0,028 in group 1 to 2 comparison, p=0,002 in comparison group 2 to groups 3 and 4, p=0 in other comparisons as shown in Table 7). Group 6 (27 ±0) was significant different to group 3 (23 ±1) (p=0,006), 4 (23 ±1) (p=0) and 5 (24 ±1) (p=0,026).

3.2.2.2.8 Right occipitomastoid suture OES in a group by group comparison

Right occipitomastoid suture showed a significant difference (p=0) in means of OES between group 6 (24 ±1) and group 1 (9 ±0), 3 (15 ±2), 4 (16 ±1) and 5 (15 ±1). No other

group-by-group comparison showed significance. Mean score of group 2 was 16 ± 1 as shown in Table 8.

3.2.2.2.9 Left occipitomastoid suture OES in a group by group comparison

Means of left occipitomastoid suture showed a difference between group 6 (23 ± 1) compared to all the younger groups 1 (9 ± 0) ($p=0$), 2 (13 ± 4) ($p=0,014$), 3 (16 ± 1) ($p=0,001$), 4 (13 ± 1) ($p=0$), and 5 (15 ± 1) ($p=0$). No significance was found in other group-by-group comparisons for this suture score.

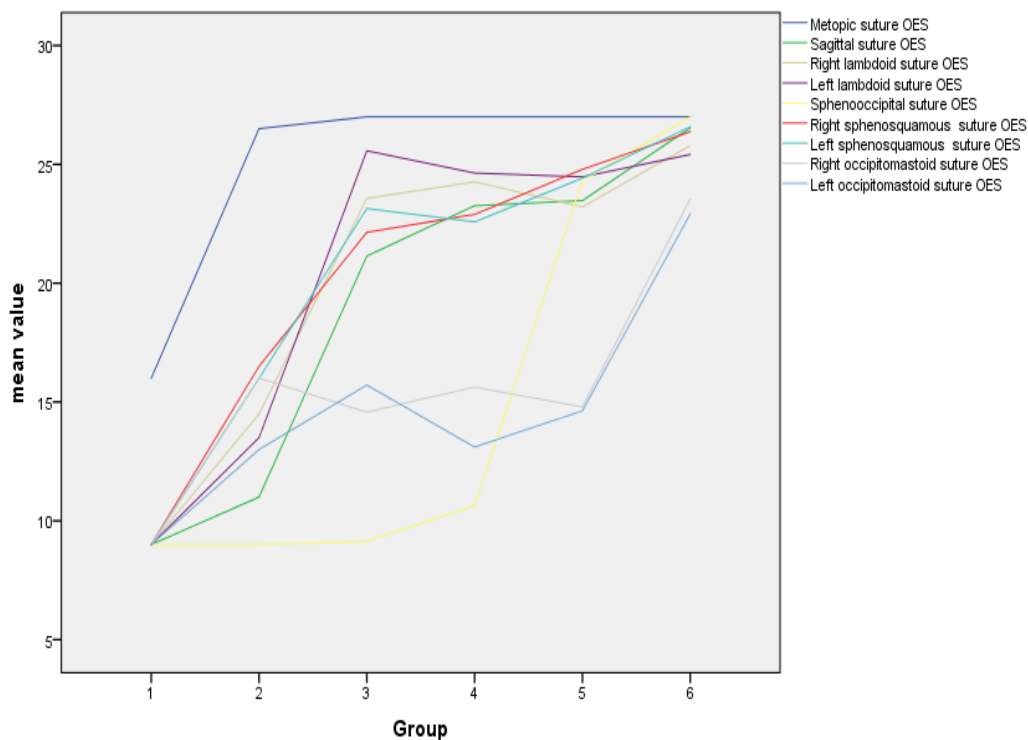


Figure 15 Line graph showing mean value of suture OES points of each group of CT patients.

		Quadratsumme	df	Mittel der Quadrate	F	Signifikanz
Metopic suture OES	Zwischen den Gruppen	235,253	5	47,051	32,004	,000
	Innerhalb der Gruppen	98,500	67	1,470		
	Gesamt	333,753	72			
Sagittal suture OES	Zwischen den Gruppen	994,928	5	198,986	23,096	,000
	Innerhalb der Gruppen	577,237	67	8,615		
	Gesamt	1572,164	72			
Right lambdoid suture OES	Zwischen den Gruppen	717,040	5	143,408	20,933	,000
	Innerhalb der Gruppen	459,015	67	6,851		
	Gesamt	1176,055	72			
Left lambdoid suture OES	Zwischen den Gruppen	744,712	5	148,942	16,435	,000
	Innerhalb der Gruppen	607,206	67	9,063		
	Gesamt	1351,918	72			
Sphenoccipital suture OES	Zwischen den Gruppen	4475,055	5	895,011	86,733	,000
	Innerhalb der Gruppen	691,383	67	10,319		
	Gesamt	5166,438	72			
Right sphenosquamous suture OES	Zwischen den Gruppen	756,399	5	151,280	30,353	,000
	Innerhalb der Gruppen	333,930	67	4,984		
	Gesamt	1090,329	72			
Left sphenosquamous suture OES	Zwischen den Gruppen	783,937	5	156,787	33,674	,000
	Innerhalb der Gruppen	311,954	67	4,656		
	Gesamt	1095,890	72			
Right occipitomastoid suture OES	Zwischen den Gruppen	1286,803	5	257,361	14,926	,000
	Innerhalb der Gruppen	1155,252	67	17,243		
	Gesamt	2442,055	72			
Left occipitomastoid suture OES	Zwischen den Gruppen	1405,158	5	281,032	18,689	,000
	Innerhalb der Gruppen	1007,472	67	15,037		
	Gesamt	2412,630	72			

Table 6 Univariate ANOVA results for suture scores of CT patients (German designations).

Abhängige Variable	(I) Group	(J) Group	Mittlere Differenz (I-J)	Standardfehler	Signifikanz
Metopic suture OES	1	2	-10,500*	1,212	,000
		3	-11,000*	,972	,000
		4	-11,000*	,901	,000
		5	-11,000*	,901	,000
		6	-11,000*	,892	,000
		2	1	10,500*	1,212
	3		-,500	,972	1,000
	4		-,500	,901	1,000
	5		-,500	,901	1,000
	6		-,500	,892	1,000
	3		1	11,000*	,972
		2	,500	,972	1,000
		4	,000	,536	1,000
		5	,000	,536	1,000
		6	,000	,521	1,000
		4	1	11,000*	,901
	2		,500	,901	1,000
	3		,000	,536	1,000
	5		,000	,393	1,000
	6		,000	,372	1,000
	5		1	11,000*	,901
		2	,500	,901	1,000
		3	,000	,536	1,000
		4	,000	,393	1,000
6		,000	,372	1,000	
6		1	11,000*	,892	,000
	2	,500	,892	1,000	
	3	,000	,521	1,000	
	4	,000	,372	1,000	
	5	,000	,372	1,000	
	Sagittal suture OES	1	2	-2,000	2,935
3			-12,143*	2,353	,000
4			-14,263*	2,182	,000
5			-14,474*	2,182	,000
6			-17,542*	2,160	,000
2			1	2,000	2,935
		3	-10,143*	2,353	,001
		4	-12,263*	2,182	,000
		5	-12,474*	2,182	,000
		6	-15,542*	2,160	,000
		3	1	12,143*	2,353
2			10,143*	2,353	,001
4			-2,120	1,298	1,000
5			-2,331	1,298	1,000
6			-5,399*	1,261	,001
4			1	14,263*	2,182
		2	12,263*	2,182	,000

		3	2,120	1,298	1,000
		5	,211	952	1,000
		6	-3,279*	901	,008
5		1	14,474*	2,182	,000
		2	12,474*	2,182	,000
		3	2,331	1,298	1,000
		4	,211	952	1,000
		6	-3,068*	901	,017
6		1	17,542*	2,160	,000
		2	15,542*	2,160	,000
		3	5,399*	1,261	,001
		4	3,279*	901	,008
		5	3,068*	901	,017
Right lambdoid suture OES	1	2	-5,500	2,617	,591
		3	-14,571*	2,099	,000
		4	-15,263*	1,946	,000
		5	-14,211*	1,946	,000
		6	-16,792*	1,926	,000
	2	1	5,500	2,617	,591
		3	-9,071*	2,099	,001
		4	-9,763*	1,946	,000
		5	-8,711*	1,946	,000
		6	-11,292*	1,926	,000
	3	1	14,571*	2,099	,000
		2	9,071*	2,099	,001
		4	-,692	1,157	1,000
		5	,361	1,157	1,000
		6	-2,220	1,124	,786
	4	1	15,263*	1,946	,000
		2	9,763*	1,946	,000
		3	,692	1,157	1,000
		5	1,053	,849	1,000
		6	-1,529	,804	,923
	5	1	14,211*	1,946	,000
		2	8,711*	1,946	,000
		3	-,361	1,157	1,000
		4	-1,053	,849	1,000
		6	-2,581*	,804	,030
	6	1	16,792*	1,926	,000
		2	11,292*	1,926	,000
		3	2,220	1,124	,786
		4	1,529	,804	,923
		5	2,581*	,804	,030
Left lambdoid suture OES	1	2	-4,500	3,010	1,000
		3	-16,571*	2,414	,000
		4	-15,632*	2,238	,000
		5	-15,474*	2,238	,000
		6	-16,417*	2,216	,000
	2	1	4,500	3,010	1,000
		3	-12,071*	2,414	,000
		4	-11,132*	2,238	,000
		5	-10,974*	2,238	,000
		6	-11,917*	2,216	,000
	3	1	16,571*	2,414	,000
		2	12,071*	2,414	,000
		4	,940	1,331	1,000
		5	1,098	1,331	1,000
		6	155	1,293	1,000
	4	1	15,632*	2,238	,000
		2	11,132*	2,238	,000
		3	,940	1,331	1,000
		5	,158	977	1,000
		6	-,785	924	1,000
	5	1	15,474*	2,238	,000
		2	10,974*	2,238	,000
		3	-1,098	1,331	1,000
		4	-,158	977	1,000
		6	-,943	924	1,000
	6	1	16,417*	2,216	,000
		2	11,917*	2,216	,000
		3	-,155	1,293	1,000
		4	,785	924	1,000
		5	943	924	1,000
Sphenooccipital suture OES	1	2	,000	3,212	1,000
		3	-,143	2,576	1,000
		4	-1,632	2,388	1,000
		5	-15,316*	2,388	,000
		6	-18,000*	2,364	,000
	2	1	,000	3,212	1,000
		3	-,143	2,576	1,000
		4	-1,632	2,388	1,000
		5	-15,316*	2,388	,000
		6	-18,000*	2,364	,000
	3	1	,143	2,576	1,000

		2	143	2,576	1,000
		4	-1,489	1,420	1,000
		5	-15,173*	1,420	1,000
		6	-17,857*	1,380	1,000
4		1	1,632	2,388	1,000
		2	1,632	2,388	1,000
		3	1,489	1,420	1,000
		5	-13,684*	1,042	1,000
		6	-16,368*	986	1,000
5		1	15,316*	2,388	1,000
		2	15,316*	2,388	1,000
		3	15,173*	1,420	1,000
		4	13,684*	1,042	1,000
		6	-2,684	986	124
6		1	18,000*	2,364	1,000
		2	18,000*	2,364	1,000
		3	17,857*	1,380	1,000
		4	16,368*	986	1,000
		5	2,684	986	124
Right sphenosquamous suture OES	1	2	-7,500*	2,232	1,019
		3	-13,143*	1,790	1,000
		4	-13,895*	1,660	1,000
		5	-15,789*	1,660	1,000
		6	-17,375*	1,643	1,000
	2	1	7,500*	2,232	1,019
		3	-5,643*	1,790	1,036
		4	-6,395*	1,660	1,004
		5	-8,289*	1,660	1,000
		6	-9,875*	1,643	1,000
	3	1	13,143*	1,790	1,000
		2	5,643*	1,790	1,036
		4	-752	987	1,000
		5	-2,647	987	1,138
		6	-4,232*	959	1,001
	4	1	13,895*	1,660	1,000
		2	6,395*	1,660	1,004
		3	752	987	1,000
		5	-1,895	724	1,165
		6	-3,480*	686	1,000
	5	1	15,789*	1,660	1,000
		2	8,289*	1,660	1,000
		3	2,647	987	1,138
		4	1,895	724	1,165
		6	-1,586	686	1,357
	6	1	17,375*	1,643	1,000
		2	9,875*	1,643	1,000
		3	4,232*	959	1,001
		4	3,480*	686	1,000
		5	1,586	686	1,357
Left sphenosquamous suture OES	1	2	-7,000*	2,158	1,028
		3	-14,143*	1,730	1,000
		4	-13,579*	1,604	1,000
		5	-15,421*	1,604	1,000
		6	-17,583*	1,588	1,000
	2	1	7,000*	2,158	1,028
		3	-7,143*	1,730	1,002
		4	-6,579*	1,604	1,002
		5	-8,421*	1,604	1,000
		6	-10,583*	1,588	1,000
	3	1	14,143*	1,730	1,000
		2	7,143*	1,730	1,002
		4	564	954	1,000
		5	-1,278	954	1,000
		6	-3,440*	927	1,006
	4	1	13,579*	1,604	1,000
		2	6,579*	1,604	1,002
		3	-564	954	1,000
		5	-1,842	700	1,158
		6	-4,004*	663	1,000
	5	1	15,421*	1,604	1,000
		2	8,421*	1,604	1,000
		3	1,278	954	1,000
		4	1,842	700	1,158
		6	-2,162*	663	1,026
	6	1	17,583*	1,588	1,000
		2	10,583*	1,588	1,000
		3	3,440*	927	1,006
		4	4,004*	663	1,000
		5	2,162*	663	1,026
Right occipitomastoid suture OES	1	2	-7,000	4,152	1,000
		3	-5,571	3,329	1,000
		4	-6,632	3,087	1,530
		5	-5,789	3,087	1,976
		6	-14,542*	3,056	1,000

2	1	7,000	4,152	1,000	
	3	1,429	3,329	1,000	
	4	368	3,087	1,000	
	5	1,211	3,087	1,000	
	6	7,542	3,056	242	
	3	1	5,571	3,329	1,000
2		-1,429	3,329	1,000	
4		-1,060	1,836	1,000	
5		-218	1,836	1,000	
6		8,970*	1,784	000	
4		1	6,632	3,087	530
	2	368	3,087	1,000	
	3	1,060	1,836	1,000	
	5	842	1,347	1,000	
	6	7,910*	1,275	000	
	5	1	5,789	3,087	976
2		-1,211	3,087	1,000	
3		218	1,836	1,000	
4		842	1,347	1,000	
6		8,752*	1,275	000	
6		1	14,542*	3,056	000
	2	7,542	3,056	242	
	3	8,970*	1,784	000	
	4	7,910*	1,275	000	
	5	8,752*	1,275	000	
	Left occipitomastoid suture OES	1	2	-4,000	3,878
3			-6,714	3,109	516
4			-4,105	2,883	1,000
5			-5,632	2,883	824
6			-13,917*	2,854	000
2			1	4,000	3,878
		3	-2,714	3,109	1,000
		4	-1,105	2,883	1,000
		5	-1,632	2,883	1,000
		6	-9,917*	2,854	014
		3	1	6,714	3,109
2			2,714	3,109	1,000
4			2,609	1,715	1,000
5			1,083	1,715	1,000
6			-7,202*	1,666	001
4			1	4,105	2,883
		2	1,105	2,883	1,000
		3	-2,609	1,715	1,000
		5	-1,526	1,258	1,000
		6	-9,811*	1,191	000
		5	1	5,632	2,883
2			1,632	2,883	1,000
3			-1,083	1,715	1,000
4			1,526	1,258	1,000
6	-8,285*		1,191	000	
6	1		13,917*	2,854	000
	2	9,917*	2,854	014	
	3	7,202*	1,666	001	
	4	9,811*	1,191	000	
	5	8,285*	1,191	000	

*. Die Differenz der Mittelwerte ist auf dem Niveau 0.05 signifikant.

Table 7 Bonferroni Post-Hoc-test results for group-by-group comparison of suture score (German designations).

Group		OES total	OES skull cap	OES skull base	M OES	S OES	L OES	R OES	SO OES	SS OES	ISS OES	OM OES	IOM OES
1	Mittelwert	88,00	43,00	45,00	16,00	9,00	9,00	9,00	9,00	9,00	9,00	9,00	9,00
	N	2	2	2	2	2	2	2	2	2	2	2	2
	Standardabweichung	9,899	9,899	1,000	9,899	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000
	Standardfehler des Mittelwertes	7,000	7,000	1,000	7,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000
2	Mittelwert	136,00	65,50	70,50	26,50	11,00	14,50	13,50	9,00	16,50	16,00	16,00	13,00
	N	2	2	2	2	2	2	2	2	2	2	2	2
	Standardabweichung	18,385	13,435	4,950	17,07	1,414	4,950	6,364	1,000	2,121	1,000	1,414	5,657
	Standardfehler des Mittelwertes	13,000	9,500	3,500	15,000	1,000	3,500	4,500	1,000	1,500	1,000	1,000	4,000
3	Mittelwert	182,00	97,29	84,71	27,00	21,14	23,57	25,57	9,14	22,14	23,14	14,57	15,71
	N	7	7	7	7	7	7	7	7	7	7	7	7
	Standardabweichung	7,211	5,219	10,095	1,000	5,113	1,718	1,134	378	2,410	2,116	5,442	3,450
	Standardfehler des Mittelwertes	2,726	1,973	3,815	1,000	1,933	649	429	143	911	800	2,057	1,304
4	Mittelwert	184,00	99,16	84,84	27,00	23,26	24,26	24,63	10,63	22,89	22,58	15,63	13,11
	N	19	19	19	19	19	19	19	19	19	19	19	19
	Standardabweichung	13,601	7,065	8,675	1,000	3,297	3,124	3,847	1,978	2,942	2,673	4,549	3,315
	Standardfehler des Mittelwertes	3,120	1,621	1,990	1,000	756	717	883	454	675	613	1,044	760
5	Mittelwert	201,11	98,16	102,95	27,00	23,47	23,21	24,47	24,32	24,79	24,42	14,79	14,63
	N	19	19	19	19	19	19	19	19	19	19	19	19
	Standardabweichung	15,734	6,858	13,493	1,000	3,389	2,820	2,855	5,869	2,226	2,775	4,529	4,487
	Standardfehler des Mittelwertes	3,610	1,573	3,095	1,000	777	647	655	1,347	511	637	1,039	1,029
6	Mittelwert	231,17	104,75	126,42	27,00	26,54	25,79	25,42	27,00	26,37	26,58	23,54	22,92
	N	24	24	24	24	24	24	24	24	24	24	24	24
	Standardabweichung	7,057	3,937	6,128	1,000	833	2,064	2,518	1,000	1,469	881	3,189	3,866
	Standardfehler des Mittelwertes	1,440	804	1,251	1,000	170	421	514	1,000	300	180	651	789
Insgesamt	Mittelwert	199,82	98,10	101,73	26,68	23,47	23,74	24,21	19,34	23,90	23,88	17,74	16,86
	N	73	73	73	73	73	73	73	73	73	73	73	73
	Standardabweichung	31,934	12,817	22,552	2,153	4,673	4,042	4,333	8,471	3,891	3,901	5,824	5,789
	Standardfehler des Mittelwertes	3,738	1,500	2,640	252	547	473	507	991	455	457	682	678

Table 8 Descriptive statistics showing mean values of total OES, skull cap OES, skull base OES and suture OES of CT patients per group (German designations).

3.2.3 <18 vs >18 years

One target figure was the deterrent of age in adults (age 18-99 years) and adolescents (age 14 to <18 years).

To especially reveal differences in suture ossification between adults and adolescents, OES of group 5 and 6 were compared. There was a significant difference in means of total OES ($p=0$), in means of skull cap OES ($p=0,013$) and in means of skull base OES ($p=0$) between the two groups. In means of the occipitomastoid suture score ($p=0$), means of the left sphenosquamous suture score ($p=0,026$), means of the right lambdoid suture score ($p=0,03$) and means of the sagittal suture score ($p=0,017$) there was a significant difference in the group 5 to group 6 comparison.

3.2.4 Female vs. male

The mean of total OES points in all male CT patients was 194 ± 5 . In all female CT patients, the mean of total OES points was 209 ± 6 as shown in Table 9.

The mean of skull cap OES points in all male CT patients was 97 ± 2 . In all female CT patients, the mean of skull cap OES points was 100 ± 2 .

The mean of skull base OES points in all male CT patients was 97 ± 3 . In all female CT patients, the mean of skull base OES points was 109 ± 4 .

The higher mean value of female patients was illustrated in boxplot graphs Figure 12 and Figure 14.

To compare distribution of score points in female and male study population Mann-Whitney-tests were applied on points of total OES, skull cap OES and skull base OES. It showed a significant gender aspect in distribution of total OES points ($p=0,017$) and skull base OES points ($p=0,026$). The OES skull cap points showed no significant difference in distribution in male and female ($p=0,145$).

Descriptive statistic results showing mean values of total OES, mean values of skull cap OES and mean values of skull base OES of CT patients separated by gender were listed in Table 9. Mann Whitney test results of comparing distribution of total OES, skull cap OES and skull base OES in male to female were shown in Table 10. The statistical significance of the test results was listed in Table 11.

An illustration of total OES points, skull cap OES points and skull base OES points separated by gender was given in Figure 12, Figure 13 and Figure 14.

sex		OES total	OES skull cap	OES skull base
male	Mittelwert	194,37	96,93	97,43
	N	46	46	46
	Standardabweichung	31,061	13,493	21,729
	Standardfehler des Mittelwertes	4,580	1,989	3,204
female	Mittelwert	209,11	100,07	109,04
	N	27	27	27
	Standardabweichung	31,811	11,549	22,430
	Standardfehler des Mittelwertes	6,122	2,223	4,317
insgesamt	Mittelwert	199,82	98,10	101,73
	N	73	73	73
	Standardabweichung	31,934	12,817	22,552
	Standardfehler des Mittelwertes	3,738	1,500	2,640

Table 9 Descriptive statistics showing mean values of total OES, skull cap OES and skull base OES of CT patients separated by gender (German designations).

	sex	N	Mittlerer Rang	Rangsumme
OES total	male	46	32,48	1494,00
	female	27	44,70	1207,00
	Gesamt	73		
OES skull cap	male	46	34,24	1575,00
	female	27	41,70	1126,00
	Gesamt	73		
OES skull base	male	46	32,77	1507,50
	female	27	44,20	1193,50
	Gesamt	73		

Table 10 Mann Whitney Test results for gender aspects in total OES, skull cap OES and skull base OES of CT measurements (German designations).

	OES total	OES skull cap	OES skull base
Mann-Whitney-U	413,000	494,000	426,500
Wilcoxon-W	1494,000	1575,000	1507,500
Z	-2,378	-1,456	-2,224
Asymptotische Signifikanz (2-seitig)	.017	.145	.026
Exakte Signifikanz (2-seitig)	.017	.147	.026
Exakte Signifikanz (1-seitig)	.008	.074	.013
Punkt-Wahrscheinlichkeit	.000	.001	.000
Gruppenvariable: sex			

Table 11 Statistics for Table 10 showing the statistical significance (German designations).

3.2.5 Right vs Left sutures

To evaluate a difference in ossification between right and left side of lambdoid suture, between right and left side of sphenosquamous suture and between right and left side of occipitomastoid suture Wilcoxon-tests were applied. There was neither a significant difference between related sides of the lambdoid suture score ($p=0,105$), nor between related sides of the sphenosquamous suture score ($p=0,815$), nor between related sides of the occipitomastoid suture score ($p=0,15$).

Wilcoxon test results of comparing OES of related sides of the lambdoid suture, of related sides of the sphenosquamous suture and of related sides of the occipitomastoid suture were shown in Table 12.

The statistical significance of the test results was listed in Table 13.

	N	Mittlerer Rang	Rangsumme
Left lambdoid suture OES - Right lambdoid suture OES	Negative Ränge	19 ^a	411,50
	Positive Ränge	28 ^b	716,50
	Bindungen	26 ^c	
	Gesamt	73	
Left sphenosquamous suture OES - Right sphenosquamous suture OES	Negative Ränge	26 ^d	661,50
	Positive Ränge	24 ^e	613,50
	Bindungen	23 ^f	
	Gesamt	73	
Left occipitomastoid suture OES - Right occipitomastoid suture OES	Negative Ränge	35 ^g	1181,50
	Positive Ränge	27 ^h	771,50
	Bindungen	11 ⁱ	
	Gesamt	73	

a. Left lambdoid suture OES < Right lambdoid suture OES b. Left lambdoid suture OES > Right lambdoid suture OES c. Left lambdoid suture OES = Right lambdoid suture OES d. Left sphenosquamous suture OES < Right sphenosquamous suture OES e. Left sphenosquamous suture OES > Right sphenosquamous suture OES f. Left sphenosquamous suture OES = Right sphenosquamous suture OES g. Left occipitomastoid suture OES < Right occipitomastoid suture OES h. Left occipitomastoid suture OES > Right occipitomastoid suture OES i. Left occipitomastoid suture OES = Right occipitomastoid suture OES

Table 12 Wilcoxon test results of comparing left and right side of lambdoid suture OES, right and left side of sphenosquamous suture OES and right and left side of occipitomastoid suture OES (German designations).

	Left lambdoid suture OES - Right lambdoid suture OES	Left sphenosquamous suture OES - Right sphenosquamous suture OES	Left occipitomastoid suture OES - Right occipitomastoid suture OES
Z	-1,623 ^b	-,235 ^c	-1,441 ^c
Asymptotische Signifikanz (2-seitig)	,105	,815	,150
Exakte Signifikanz (2-seitig)	,106	,818	,151
Exakte Signifikanz (1-seitig)	,053	,409	,075
Punkt-Wahrscheinlichkeit	,001	,003	,001

b. Basiert auf negativen Rängen. c. Basiert auf positiven Rängen.

Table 13 Statistics for Table 12 showing the statistical significance (German designations).

3.2.6 Suture width

To receive suture width data, at each CT measurement point the length measurement in mm between two bones was saved. The suture width was defined as gap between two compact bones.

The mean width of each suture showed the highest value in group 1. The metopic suture, the sagittal suture and the sphenoccipital suture showed a continuous decrease of width.

The lowest mean width of the sutures was found in group 6, except for the left lambdoid suture which showed the lowest mean width in group 3.

An illustration of the mean suture width of each group of CT patients was given in Figure 16.

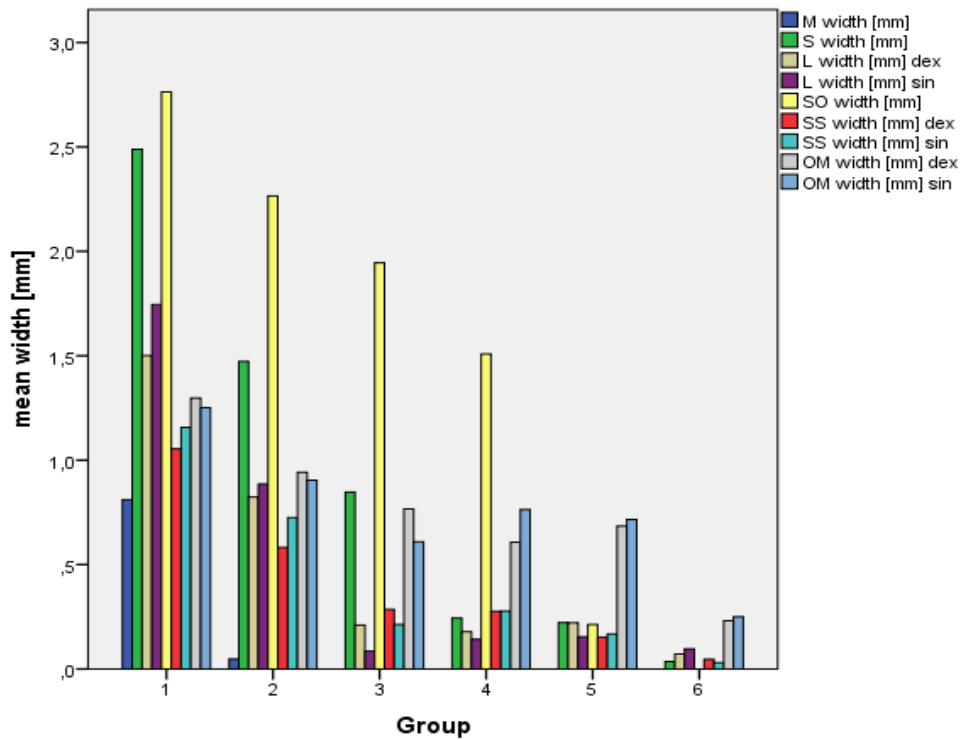


Figure 16 Bar graph showing means of width of each suture per group in CT patients.

3.3 MRI results

3.3.1 OES vs SES (in MRI patients)

Wilcoxon tests showed a difference between means of objective and means of subjective evaluation in total score ($p=0,005$), skull cap score ($p=0,001$) and skull base score ($p=0,035$).

Descriptive statistic results showing mean values of total OES, total SES, skull cap OES, skull cap SES, skull base OES and skull base SES of MRI patients were listed in Table 14. Wilcoxon test results of comparing total OES to total SES, skull cap OES to skull cap SES and skull base OES to skull base SES were shown in Table 15. The statistical significance of the test results was listed in Table 16.

An illustration of the mean values of total OES and mean values of total SES per group was given in a scatterplot in Figure 17 and in a line graph in Figure 18.

Due to these results and due to better reproducibility of objective evaluations the OES points were used for further testing.

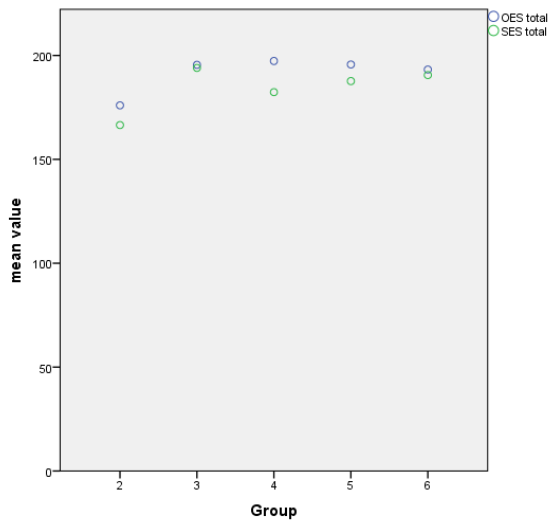


Figure 17 Scatterplot showing means of total OES points and means of total SES points of each group of MRI patients.

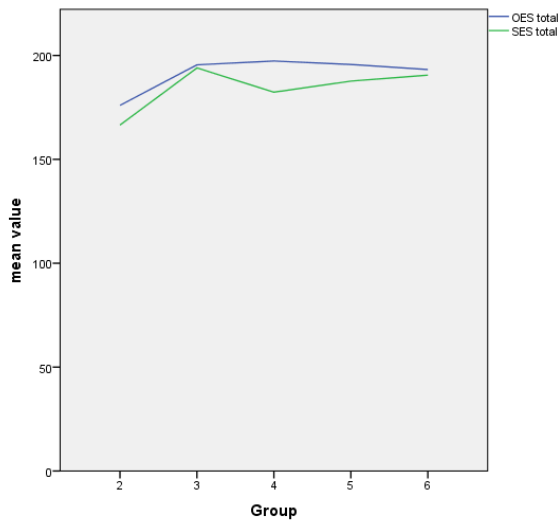


Figure 18 Line graph showing means of total OES points and means of total SES points of each group of MRI patients.

	N	Minimum	Maximum	Mittelwert	Standardabweichung
OES total	26	151	240	193,12	21,263
SES total	26	156	220	187,35	15,476
OES skull cap	26	71	108	91,85	10,267
SES skull cap	26	75	104	88,81	8,222
OES skull base	26	80	132	101,27	13,062
SES skull base	26	81	121	98,54	9,153
Gültige Werte (Listenweise)	26				

Table 14 Descriptive statistics showing mean values of total OES, total SES, skull cap OES, skull cap SES, skull base OES and skull base SES of MRI patients (German designations).

		N	Mittlerer Rang	Rangsumme
SES total - OES total	Negative Ränge	18 ^a	14,86	267,50
	Positive Ränge	7 ^b	8,21	57,50
	Bindungen	1 ^c		
	Gesamt	26		
SES skull cap - OES skull cap	Negative Ränge	18 ^d	14,50	261,00
	Positive Ränge	6 ^e	6,50	39,00
	Bindungen	2 ^f		
	Gesamt	26		
SES skull base - OES skull base	Negative Ränge	18 ^g	12,42	223,50
	Positive Ränge	6 ^h	12,75	76,50
	Bindungen	2 ⁱ		
	Gesamt	26		

a. SES total < OES total b. SES total > OES total c. SES total = OES total d. SES skull cap < OES skull cap e. SES skull cap > OES skull cap f. SES skull cap = OES skull cap g. SES skull base < OES skull base h. SES skull base > OES skull base i. SES skull base = OES skull base

Table 15 Wilcoxon test results of comparing total OES to total SES, skull cap OES to skull cap SES and skull base OES to skull base SES in MRI patients (German designations).

	SES total - OES total	SES skull cap - OES skull cap	SES skull base - OES skull base
Z	-2,827b	-3,178b	-2,106b
Asymptotische Signifikanz (2-seitig)	,005	,001	,035
Exakte Signifikanz (2-seitig)	,003	,001	,034
Exakte Signifikanz (1-seitig)	,002	,000	,017
Punkt-Wahrscheinlichkeit	,000	,000	,001

b. Basiert auf positiven Rängen.

Table 16 Statistic results for Table 15 showing the statistical significance (German designations).

3.3.2 Group vs Group (in MRI patients)

3.3.2.1 Total OES, skull cap OES and skull base in a group by group comparison (in MRI patients)

There were no significant differences calculable in means of total score ($p=1$), means of skull cap score ($p=0,993$ in group 2 to group 6 comparison, $p=1$ in other comparisons as shown in Table 18) and in means of skull base score ($p=1$) in group-by-group comparisons. Descriptive statistic results showing mean values of total OES, skull cap OES and skull base OES of MRI patients were listed in Table 21.

Univariate ANOVA results of total OES, skull cap OES and skull base OES were shown in Table 17. The Bonferroni Post-Hoc test results comparing means of total OES, means of skull cap OES and means of skull base OES by group were shown Table 18.

An illustration of total OES points per group separated by gender was given in the boxplot graph Figure 19, of skull cap OES points in the boxplot in Figure 20 and of skull base OES points in the boxplot Figure 21.

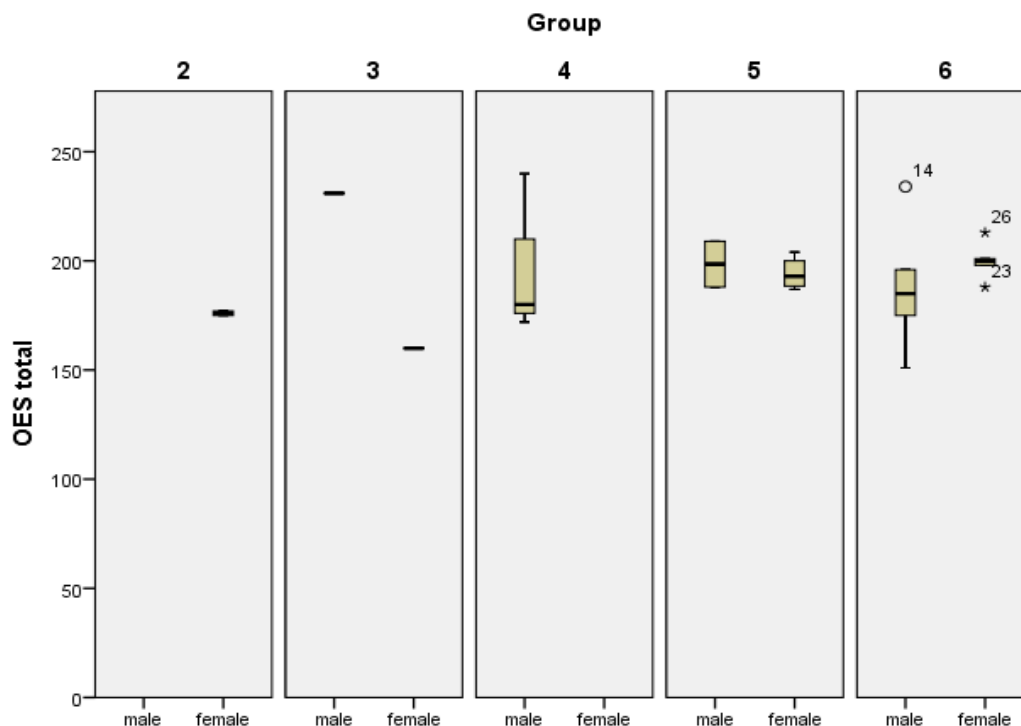


Figure 19 Boxplot showing total OES points of male and female MRI patients of each group.

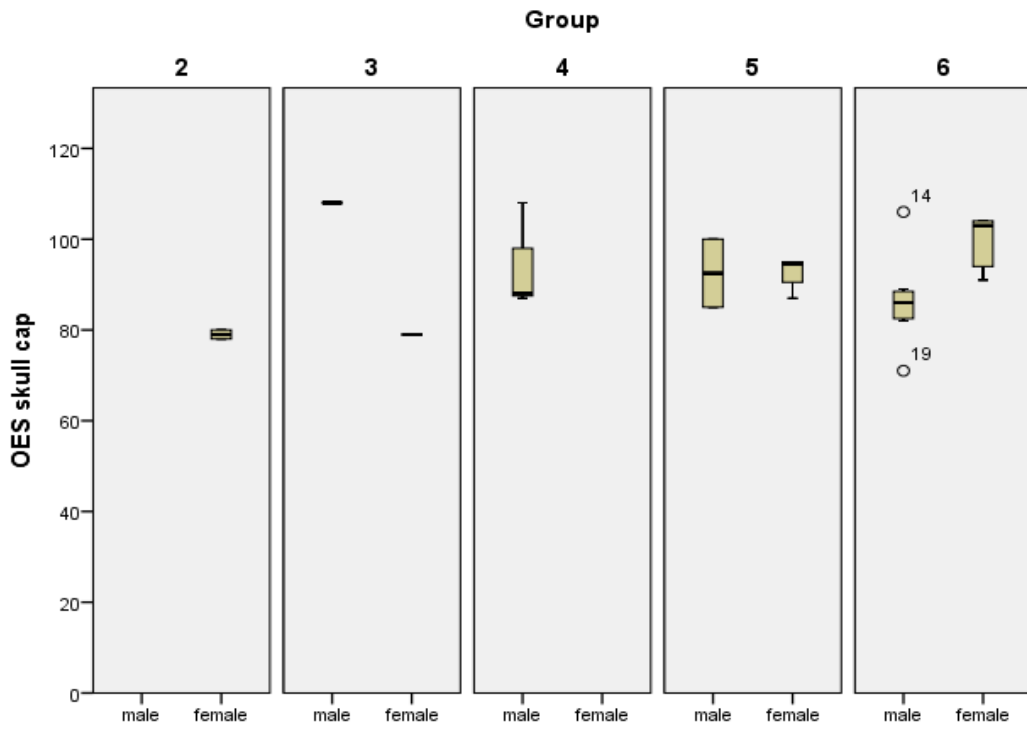


Figure 20 Boxplot showing skull cap OES points of male and female MRI patients of each group.

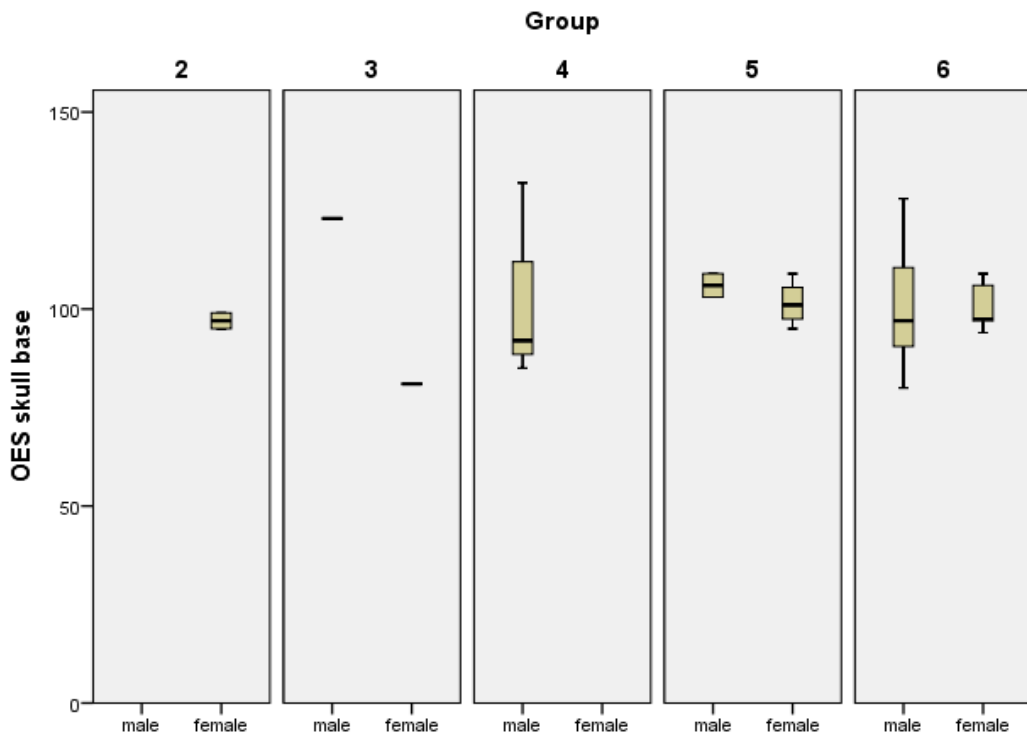


Figure 21 Boxplot showing skull base OES points of male and female MRI patients of each group.

		Quadratsumme	df	Mittel der Quadrate	F	Signifikanz
OES total	Zwischen den Gruppen	689,846	4	172,462	,341	,847
	Innerhalb der Gruppen	10612,808	21	505,372		
	Gesamt	11302,654	25			
OES skull cap	Zwischen den Gruppen	365,808	4	91,452	,846	,512
	Innerhalb der Gruppen	2269,577	21	108,075		
	Gesamt	2635,385	25			
OES skull base	Zwischen den Gruppen	70,038	4	17,510	,088	,985
	Innerhalb der Gruppen	4195,077	21	199,766		
	Gesamt	4265,115	25			

Table 17 Univariate ANOVA results for total OES, skull cap OES and skull base OES of MRI patients (German designations).

Abhängige Variable	(I) Group	(J) Group	Mittlere Differenz (I-J)	Standardfehler	Signifikanz	
OES total	2	3	-19,500	22,480	1,000	
		4	-21,333	20,522	1,000	
		5	-19,667	18,355	1,000	
		6	-17,231	17,075	1,000	
	3	2	19,500	22,480	1,000	
		4	-1,833	20,522	1,000	
		5	-,167	18,355	1,000	
		6	2,269	17,075	1,000	
	4	2	21,333	20,522	1,000	
		3	1,833	20,522	1,000	
		5	1,667	15,896	1,000	
		6	4,103	14,399	1,000	
	5	2	19,667	18,355	1,000	
		3	-,167	18,355	1,000	
		4	-1,667	15,896	1,000	
		6	2,436	11,095	1,000	
	6	2	17,231	17,075	1,000	
		3	-2,269	17,075	1,000	
		4	-4,103	14,399	1,000	
		5	-2,436	11,095	1,000	
	OES skull cap	2	3	-14,500	10,396	1,000
			4	-15,333	9,490	1,000
			5	-13,667	8,488	1,000
			6	-13,615	7,896	,993
3		2	14,500	10,396	1,000	
		4	-,833	9,490	1,000	
		5	,833	8,488	1,000	
		6	,885	7,896	1,000	
4		2	15,333	9,490	1,000	
		3	,833	9,490	1,000	
		5	1,667	7,351	1,000	
		6	1,718	6,659	1,000	
5		2	13,667	8,488	1,000	
		3	-,833	8,488	1,000	
		4	-1,667	7,351	1,000	
		6	,051	5,131	1,000	
6		2	13,615	7,896	,993	
		3	-,885	7,896	1,000	
		4	-1,718	6,659	1,000	
		5	-,051	5,131	1,000	
OES skull base		2	3	-5,000	14,134	1,000
			4	-6,000	12,902	1,000
			5	-6,000	11,540	1,000
			6	-3,615	10,735	1,000
	3	2	5,000	14,134	1,000	
		4	-1,000	12,902	1,000	
		5	-1,000	11,540	1,000	
		6	1,385	10,735	1,000	
	4	2	6,000	12,902	1,000	
		3	1,000	12,902	1,000	
		5	,000	9,994	1,000	
		6	2,385	9,053	1,000	
	5	2	6,000	11,540	1,000	
		3	1,000	11,540	1,000	
		4	,000	9,994	1,000	
		6	2,385	6,976	1,000	
	6	2	3,615	10,735	1,000	
		3	-1,385	10,735	1,000	
		4	-2,385	9,053	1,000	
		5	-2,385	6,976	1,000	

Table 18 Bonferroni Post-Hoc-test results for group-by-group comparison for total OES, skull cap OES and skull base OES of MRI patients (German designations).

3.3.2.2 Suture OES in a group by group comparison (in MRI patients)

The group-by-group comparison of suture score means of each suture showed some significant results.

Descriptive statistic results showing mean values of the suture OES of each suture of MRI patients were listed in Table 21.

Univariate ANOVA results of suture scores were shown in Table 19. The Bonferroni Post-Hoc test results comparing means of suture OES by group were shown in Table 20.

An illustration of mean values of suture OES points per group was given in the line graph in Figure 22.

3.3.2.2.1 Metopic suture OES in a group by group comparison

In group 2 the mean of metopic suture score was 22 ± 4 points and showed a significant difference to the older groups ($p=0,006$ in comparison to group 3, $p=0,002$ in comparison to group 4, $p=0,001$ in comparison to group 5 and $p=0$ in comparison to group 6). Group 3 (27 ± 0), 4 (27 ± 0), 5 (27 ± 0), and 6 (27 ± 0) showed equality in score means $\pm SE$.

3.3.2.2.2 Sagittal suture OES in a group by group comparison

Means of sagittal suture score showed no significant difference in any group-by-group comparison ($p=1$).

3.3.2.2.3 Right and left lambdoid suture OES in a group by group comparison

Means of right lambdoid suture OES and left lambdoid suture OES showed no significant difference in any group-by-group comparison ($p=1$).

3.3.2.2.4 Sphenooccipital suture OES in a group by group comparison

Means of sphenooccipital suture OES showed a significant difference between group 3 (14 ± 5) and group 6 (25 ± 1) ($p=0,006$).

3.3.2.2.5 Right and left sphenosquamous suture OES and right and left occipitomastoid suture OES in a group by group comparison

Neither right sphenosquamous suture ($p=1$), nor left sphenosquamous suture ($p=1$), nor right occipitomastoid suture ($p=1$) nor left occipitomastoid suture ($p=0,851$ in group 3 to 6 comparison, $p=1$ in other comparisons as shown in Table 20) showed a difference in their score means in group-by-group comparisons.

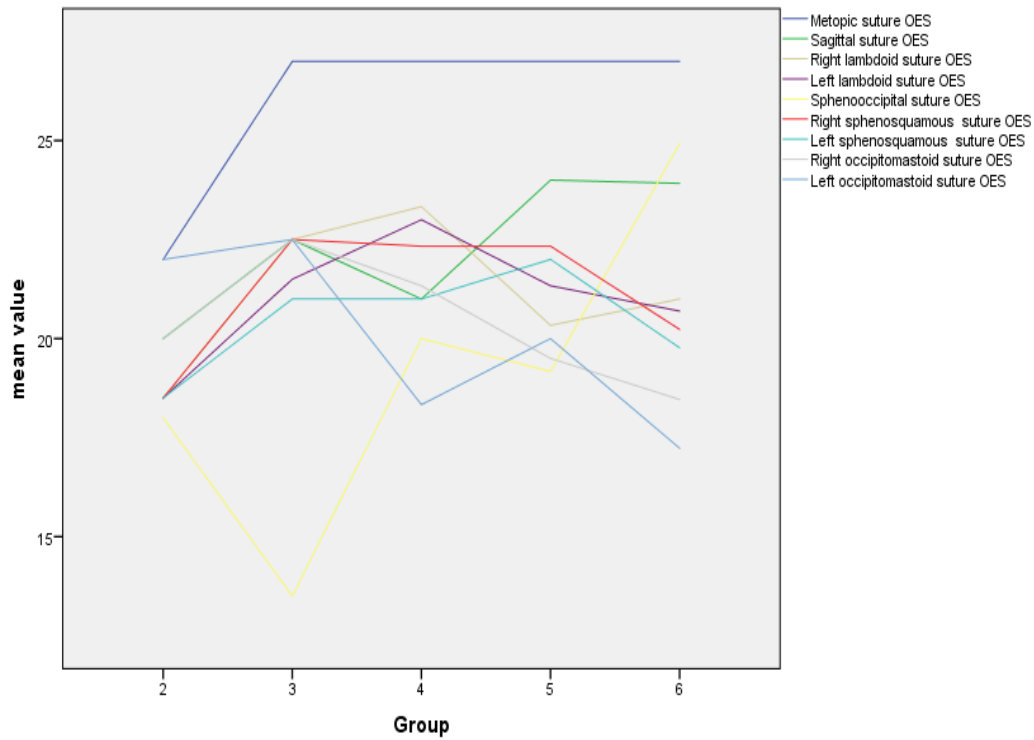


Figure 22 Line graph showing mean values of suture OES points of MRI patients of each group.

		Quadratsumme	df	Mittel der Quadrate	F	Signifikanz
Metopic suture OES	Zwischen den Gruppen	46,154	4	11,538	7,572	,001
	Innerhalb der Gruppen	32,000	21	1,524		
	Gesamt	78,154	25			
Sagittal suture OES	Zwischen den Gruppen	46,615	4	11,654	,908	,477
	Innerhalb der Gruppen	269,423	21	12,830		
	Gesamt	316,038	25			
Right lambdoid suture OES	Zwischen den Gruppen	35,962	4	8,990	,581	,680
	Innerhalb der Gruppen	325,000	21	15,476		
	Gesamt	360,962	25			
Left lambdoid suture OES	Zwischen den Gruppen	26,897	4	6,724	,343	,845
	Innerhalb der Gruppen	411,103	21	19,576		
	Gesamt	438,000	25			
Sphenooccipital suture OES	Zwischen den Gruppen	343,897	4	85,974	6,136	,002
	Innerhalb der Gruppen	294,256	21	14,012		
	Gesamt	638,154	25			
Right sphenosquamous suture OES	Zwischen den Gruppen	40,692	4	10,173	,871	,498
	Innerhalb der Gruppen	245,308	21	11,681		
	Gesamt	286,000	25			
Left sphenosquamous suture OES	Zwischen den Gruppen	29,538	4	7,385	,666	,623
	Innerhalb der Gruppen	232,808	21	11,086		
	Gesamt	262,346	25			
Right occipitomastoid suture OES	Zwischen den Gruppen	42,564	4	10,641	,793	,543
	Innerhalb der Gruppen	281,897	21	13,424		
	Gesamt	324,462	25			
Left occipitomastoid suture OES	Zwischen den Gruppen	89,141	4	22,285	1,512	,235
	Innerhalb der Gruppen	309,474	21	14,737		
	Gesamt	398,615	25			

Table 19 Univariate ANOVA results for suture scores of MRI patients (German designations).

Abhängige Variable	(I) Group	(J) Group	Mittlere Differenz (I-J)	Standardfehler	Signifikanz
Metopic suture OES	2	3	-5,000*	1,234	,006
		4	-5,000*	1,127	,002
		5	-5,000*	1,008	,001
		6	-5,000*	,938	,000
	3	2	5,000*	1,234	,006
		4	,000	1,127	1,000
		5	,000	1,008	1,000
		6	,000	,938	1,000
	4	2	5,000*	1,127	,002
		3	,000	1,127	1,000
		5	,000	,873	1,000
		6	,000	,791	1,000
	5	2	5,000*	1,008	,001
		3	,000	1,008	1,000
		4	,000	,873	1,000
		6	,000	,609	1,000
	6	2	5,000*	,938	,000
		3	,000	,938	1,000
4		,000	,791	1,000	
5		,000	,609	1,000	
Sagittal suture OES	2	3	-2,500	3,582	1,000
		4	-1,000	3,270	1,000
		5	-4,000	2,925	1,000
		6	-3,923	2,721	1,000
	3	2	2,500	3,582	1,000
		4	1,500	3,270	1,000
		5	-1,500	2,925	1,000
		6	-1,423	2,721	1,000
	4	2	1,000	3,270	1,000
		3	-1,500	3,270	1,000
		5	-3,000	2,533	1,000
		6	-2,923	2,294	1,000
	5	2	4,000	2,925	1,000
		3	1,500	2,925	1,000
		4	3,000	2,533	1,000
		6	,077	1,768	1,000
	6	2	3,923	2,721	1,000
		3	1,423	2,721	1,000
4		2,923	2,294	1,000	
5		-,077	1,768	1,000	
Right lambdoid suture OES	2	3	-4,000	3,934	1,000
		4	-4,833	3,591	1,000
		5	-1,833	3,212	1,000
		6	-2,500	2,988	1,000
	3	2	4,000	3,934	1,000
		4	-,833	3,591	1,000
		5	2,167	3,212	1,000
		6	1,500	2,988	1,000
	4	2	4,833	3,591	1,000
		3	-,833	3,591	1,000
		5	3,000	2,782	1,000
		6	2,333	2,520	1,000
	5	2	1,833	3,212	1,000
		3	-2,167	3,212	1,000
		4	-3,000	2,782	1,000
		6	-,667	1,942	1,000
	6	2	2,500	2,988	1,000
		3	-1,500	2,988	1,000
4		-2,333	2,520	1,000	
5		,667	1,942	1,000	
Left lambdoid suture OES	2	3	-3,000	4,425	1,000
		4	-4,500	4,039	1,000
		5	-2,833	3,613	1,000
		6	-2,192	3,361	1,000
	3	2	3,000	4,425	1,000
		4	-1,500	4,039	1,000
		5	,167	3,613	1,000
		6	-,808	3,361	1,000
	4	2	4,500	4,039	1,000
		3	1,500	4,039	1,000
		5	1,667	3,129	1,000
		6	2,308	2,834	1,000
	5	2	2,833	3,613	1,000
		3	-,167	3,613	1,000
		4	-1,667	3,129	1,000
		6	,641	2,184	1,000
	6	2	2,192	3,361	1,000
		3	-,808	3,361	1,000
4		-2,308	2,834	1,000	

		5	-,641	2,184	1,000
Sphenooccipital suture OES	2	3	4,500	3,743	1,000
		4	-2,000	3,417	1,000
		5	-1,167	3,056	1,000
		6	-6,923	2,843	239
	3	2	-4,500	3,743	1,000
		4	-6,500	3,417	710
		5	-5,667	3,056	778
		6	-11,423*	2,843	006
	4	2	2,000	3,417	1,000
		3	6,500	3,417	710
		5	,833	2,647	1,000
		6	-4,923	2,398	527
5	2	1,167	3,056	1,000	
	3	5,667	3,056	778	
	4	-,833	2,647	1,000	
	6	-5,756	1,847	052	
6	2	6,923	2,843	239	
	3	11,423*	2,843	006	
	4	4,923	2,398	527	
	5	5,756	1,847	052	
Right sphenosquamous suture OES	2	3	-4,000	3,418	1,000
		4	-3,833	3,120	1,000
		5	-3,833	2,791	1,000
		6	-1,731	2,596	1,000
	3	2	4,000	3,418	1,000
		4	,167	3,120	1,000
		5	,167	2,791	1,000
		6	2,269	2,596	1,000
	4	2	3,833	3,120	1,000
		3	-,167	3,120	1,000
		5	,000	2,417	1,000
		6	2,103	2,189	1,000
5	2	3,833	2,791	1,000	
	3	-,167	2,791	1,000	
	4	,000	2,417	1,000	
	6	2,103	1,687	1,000	
6	2	1,731	2,596	1,000	
	3	-2,269	2,596	1,000	
	4	-2,103	2,189	1,000	
	5	-2,103	1,687	1,000	
Left sphenosquamous suture OES	2	3	-2,500	3,330	1,000
		4	-2,500	3,039	1,000
		5	-3,500	2,719	1,000
		6	-1,269	2,529	1,000
	3	2	2,500	3,330	1,000
		4	,000	3,039	1,000
		5	-1,000	2,719	1,000
		6	1,231	2,529	1,000
	4	2	2,500	3,039	1,000
		3	,000	3,039	1,000
		5	-1,000	2,354	1,000
		6	1,231	2,133	1,000
5	2	3,500	2,719	1,000	
	3	1,000	2,719	1,000	
	4	1,000	2,354	1,000	
	6	2,231	1,643	1,000	
6	2	1,269	2,529	1,000	
	3	-1,231	2,529	1,000	
	4	-1,231	2,133	1,000	
	5	-2,231	1,643	1,000	
Right occipitomastoid suture OES	2	3	-2,500	3,664	1,000
		4	-1,333	3,345	1,000
		5	,500	2,992	1,000
		6	1,538	2,783	1,000
	3	2	2,500	3,664	1,000
		4	1,167	3,345	1,000
		5	3,000	2,992	1,000
		6	4,038	2,783	1,000
	4	2	1,333	3,345	1,000
		3	-1,167	3,345	1,000
		5	1,833	2,591	1,000
		6	2,872	2,347	1,000
5	2	-,500	2,992	1,000	
	3	-3,000	2,992	1,000	
	4	-1,833	2,591	1,000	
	6	1,038	1,808	1,000	
6	2	-1,538	2,783	1,000	
	3	-4,038	2,783	1,000	
	4	-2,872	2,347	1,000	
	5	-1,038	1,808	1,000	
Left occipitomastoid suture OES	2	3	-,500	3,839	1,000
		4	3,667	3,504	1,000

	5	2,000	3,134	1,000
	6	4,769	2,916	1,000
3	2	3,500	3,839	1,000
	4	4,167	3,504	1,000
	5	2,500	3,134	1,000
	6	5,269	2,916	851
4	2	-3,667	3,504	1,000
	3	-4,167	3,504	1,000
	5	-1,667	2,714	1,000
	6	1,103	2,459	1,000
5	2	-2,000	3,134	1,000
	3	-2,500	3,134	1,000
	4	1,667	2,714	1,000
	6	2,769	1,895	1,000
6	2	-4,769	2,916	1,000
	3	-5,269	2,916	851
	4	-1,103	2,459	1,000
	5	-2,769	1,895	1,000

Table 20 Bonferroni Post-Hoc-test results for group-by-group comparison of suture score of MRI patients (German designations).

Group	OES total	OES skull cap	OES skull base	M OES	S OES	rLL OES	rLL OES	SO OES	rSS OES	ISS OES	rOM OES	lOM OES
2 Mittelwert	176,00	79,00	97,00	22,00	20,00	18,50	18,50	18,00	18,50	18,50	20,00	22,00
N	2	2	2	2	2	2	2	2	2	2	2	2
Standardabweichung	1,414	1,414	2,828	5,657	2,828	7,07	7,07	1,000	7,07	7,07	2,828	1,000
Standardfehler des Mittelwertes	1,000	1,000	2,000	4,000	2,000	5,000	5,000	1,000	5,000	5,000	2,000	1,000
3 Mittelwert	195,50	93,50	102,00	27,00	22,50	22,50	21,50	13,50	22,50	21,00	22,50	22,50
N	2	2	2	2	2	2	2	2	2	2	2	2
Standardabweichung	50,205	20,506	29,698	1,000	6,364	6,364	7,778	6,364	6,364	4,243	6,364	6,364
Standardfehler des Mittelwertes	35,500	14,500	21,000	1,000	4,500	4,500	5,500	4,500	4,500	3,000	4,500	4,500
4 Mittelwert	197,33	94,33	103,00	27,00	21,00	23,33	23,00	20,00	22,33	21,00	21,33	18,33
N	3	3	3	3	3	3	3	3	3	3	3	3
Standardabweichung	37,166	11,846	25,357	1,000	5,196	4,041	4,583	4,359	4,509	4,359	4,933	8,505
Standardfehler des Mittelwertes	21,458	6,839	14,640	1,000	3,000	2,333	2,646	2,517	2,603	2,517	2,848	4,910
5 Mittelwert	195,67	92,67	103,00	27,00	24,00	20,33	21,33	19,17	22,33	22,00	19,50	20,00
N	6	6	6	6	6	6	6	6	6	6	6	6
Standardabweichung	9,092	5,610	5,404	1,000	2,966	1,966	2,582	4,875	2,338	2,280	1,975	2,757
Standardfehler des Mittelwertes	3,712	2,290	2,206	1,000	1,211	803	1,054	1,990	955	931	806	1,125
6 Mittelwert	193,23	92,62	100,62	27,00	23,92	21,00	20,69	24,92	20,23	19,77	18,46	17,23
N	13	13	13	13	13	13	13	13	13	13	13	13
Standardabweichung	20,237	10,836	12,494	1,000	3,201	4,397	4,785	2,842	3,370	3,539	3,711	2,682
Standardfehler des Mittelwertes	5,613	3,005	3,465	1,000	888	1,219	1,327	788	935	982	1,029	744
Insgesamt Mittelwert	193,12	91,85	101,27	26,62	23,19	21,04	21,00	21,62	21,00	20,42	19,46	18,77
Standardabweichung	21,263	10,267	13,062	1,768	3,555	3,800	4,186	5,052	3,382	3,239	3,603	3,993
Standardfehler des Mittelwertes	4,170	2,014	2,562	347	697	745	821	991	663	635	707	783

Table 21 Descriptive statistics showing mean values of total OES, skull cap OES, skull base OES and suture OES of MRI patients per group (German designations).

3.3.3 <18 vs >18 years (in MRI patients)

In MRI measurements and scoring there was no significant difference found between group 5 (adolescents <18 years) and group 6 adults (>18 years).

3.3.4 Female vs male (in MRI patients)

To compare distribution of score points in female and male study population Mann-Whitney-tests were applied on total OES, skull cap OES and skull base OES. There was no significant difference in distribution of the scores related to sex.

Descriptive statistic results showing mean values of total OES, mean values of skull cap OES and mean values of skull base OES of CT patients separated by gender were listed in Table 22. Mann Whitney test results of comparing distribution of total OES, skull cap OES and skull base OES in male to female patients were shown in Table 23. The statistical significance of the test results was listed in Table 24.

An illustration of total OES points per group separated by gender was given in a boxplot graph in Figure 19, of skull cap OES points in Figure 20 and of skull base OES points in Figure 21.

sex		OES total	OES skull cap	OES skull base
male	Mittelwert	194,77	90,85	103,92
	N	13	13	13
	Standardabweichung	27,090	11,283	16,919
	Standardfehler des Mittelwertes	7,513	3,129	4,692
female	Mittelwert	191,46	92,85	98,62
	N	13	13	13
	Standardabweichung	14,216	9,494	7,343
	Standardfehler des Mittelwertes	3,943	2,633	2,037
Insgesamt	Mittelwert	193,12	91,85	101,27
	N	26	26	26
	Standardabweichung	21,263	10,267	13,062
	Standardfehler des Mittelwertes	4,170	2,014	2,562

Table 22 Descriptive statistics showing mean values of total OES, skull cap OES and skull base OES of MRI patients separated by gender (German designations).

	sex	N	Mittlerer Rang	Rangsumme
OES total	male	13	13,12	170,50
	female	13	13,88	180,50
	Gesamt	26		
OES skull cap	male	13	12,81	166,50
	female	13	14,19	184,50
	Gesamt	26		
OES skull base	male	13	14,54	189,00
	female	13	12,46	162,00
	Gesamt	26		

Table 23 Mann Whitney Test results for gender aspects in total OES, skull cap OES and skull base OES of MRI measurements (German designations).

	OES total	OES skull cap	OES skull base
Mann-Whitney-U	79,500	75,500	71,000
Wilcoxon-W	170,500	166,500	162,000
Z	-,257	-,462	-,694
Asymptotische Signifikanz (2-seitig)	,797	,644	,488
Exakte Signifikanz [2*(1-seitige Sig.)]	,801 ^b	,650 ^b	,511 ^b
Exakte Signifikanz (2-seitig)	,811	,659	,502
Exakte Signifikanz (1-seitig)	,405	,329	,251
Punkt-Wahrscheinlichkeit	,010	,009	,008

Gruppenvariable: sex b. Nicht für Bindungen korrigiert.

Table 24 Statistics for Table 23 showing the statistical significance (German designations).

3.3.5 Right vs Left sutures (in MRI patients)

To evaluate a difference in ossification between right and left side of lambdoid suture, between right and left side of sphenosquamous suture and between right and left side of occipitomastoid suture Wilcoxon-tests were applied. There was neither a significant difference between related sides of the lambdoid suture score ($p=0,919$), nor between related sides of the sphenosquamous suture score ($p=0,315$), nor between related sides of the occipitomastoid suture score ($p=0,392$).

Wilcoxon test results of comparing OES of related sides of the lambdoid suture, of related sides of the sphenosquamous suture and of related sides of the occipitomastoid suture were shown in Table 25. The statistical significance of the test results was listed in Table 26.

	N	Mittlerer Rang	Rangsumme
Left lambdoid suture OES - Right lambdoid suture OES	Negative Ränge	10 ^a	9,75
	Positive Ränge	9 ^b	10,28
	Bindungen	7 ^c	
	Gesamt	26	
Left sphenosquamous suture OES - Right sphenosquamous suture OES	Negative Ränge	13 ^d	12,04
	Positive Ränge	9 ^e	10,72
	Bindungen	4 ^f	
	Gesamt	26	
Left occipitomastoid suture OES - Right occipitomastoid suture OES	Negative Ränge	11 ^g	8,59
	Positive Ränge	6 ^h	9,75
	Bindungen	9 ⁱ	
	Gesamt	26	

a. Left lambdoid suture OES < Right lambdoid suture OES b. Left lambdoid suture OES > Right lambdoid suture OES c. Left lambdoid suture OES = Right lambdoid suture OES d. Left sphenosquamous suture OES < Right sphenosquamous suture OES e. Left sphenosquamous suture OES > Right sphenosquamous suture OES f. Left sphenosquamous suture OES = Right sphenosquamous suture OES g. Left occipitomastoid suture OES < Right occipitomastoid suture OES h. Left occipitomastoid suture OES > Right occipitomastoid suture OES i. Left occipitomastoid suture OES = Right occipitomastoid suture OES

Table 25 Wilcoxon test results of comparing left and right side of lambdoid suture OES, right and left side of sphenosquamous suture OES and right and left side of occipitomastoid suture OES of MRI patients (German designations).

	Left lambdoid suture OES - Right lambdoid suture OES	Left sphenosquamous suture OES - Right sphenosquamous suture OES	Left occipitomastoid suture OES - Right occipitomastoid suture OES
Z	-,101 ^b	-1,005 ^b	-,856 ^b
Asymptotische Signifikanz (2-seitig)	,919	,315	,392
Exakte Signifikanz (2-seitig)	,930	,332	,410
Exakte Signifikanz (1-seitig)	,465	,166	,205
Punkt-Wahrscheinlichkeit	,010	,009	,008

b. Basiert auf positiven Rängen.

Table 26 Statistics for Table 25 showing the statistical significance (German designations).

4 DISCUSSION

4.1 Results

4.1.1 Study criteria and patients

It was a retrospective study which was based on healthy patients that at least should not have been radiological examined of the head because of suture involving diseases, such as growth disorder or endocrinal syndromes. The CT images were taken from trauma patients, because the reason for their head imaging were mainly accidents and not for example progress monitoring as in tumor patients' CT head examinations. The second reason for trauma CT analysis was the slice thickness, which had to be as thin as possible to catch sutures as wholesome as possible. In trauma CT images the slice thickness was generally 1,5mm and in most examinations, there were axial, coronal and sagittal views available to guarantee a good visualization of the suture location and to ensure divided measurements along its course. Age determination via sutures is known mainly for adult skulls. (11,20) To show age related suture ossification, this study included all ages to retrace the closing of cranial sutures.

4.1.2 Score establishment

Due to a criticized lack of objectivity in previous studies (21,22), an objective evaluation score was established for this study to quantify the analysis of the suture ossification and to increase the level of repeatability. The score was based on the special characteristics of the imaging method: In CT images the HU was defined as the objective parameter for evaluation. In MRI images the signal intensity described the suture ossification grade. Limit values of each parameter were set after comparing values of related tissues, such as soft tissue, marginal and compact bone.

To show the difference between a subjective and an objective evaluation the total OES, skull cap OES and skull base OES and its related SES scores were compared. The results of the CT measurements didn't surprise as there was a significant difference between the means of total OES and total SES, between skull cap OES and skull cap SES and between skull base OES and skull base SES ($p < 0,05$). These results reveal the importance of objectivity in the measuring methods. The objectivity is also a severe factor in the scientific request of reproducibility of a study.

4.1.3 Age assessment

Measuring in CT images, the means of total OES points in each group were significant different to each other, except for the comparison of group 3 to 4. Neither showed group 3 to 4 a significant difference in means of any other applied test.

The certain point of interest, the difference between adolescents and adults, was examined by comparing group 5 (14 to <18 years) to group 6 (18 to 99 years). Comparing the individual suture score means group by group there was a significant difference between group 5 to 6 in the mean OES of the sagittal suture and in the mean OES of each side of the occipitomastoid suture. There was an additional significant difference between group 5 and 6 in the mean OES of the left sphenosquamous suture and in the mean OES of right lambdoid suture. This shows that looking at certain sutures there can be differences found in adolescents compared to adults.

But due to overlap of lowest and highest scored points of individuals in group 5 and 6, a certain retrograde determent of age of an individual in these groups cannot be made by using score points as the only determining factor.

In certain sutures MRI measurements showed similar results compared to CT findings. The youngest patients of MRI measurements were patients of group 2. They showed a significant difference to the older groups regarding the means of metopic suture OES. In CT measurements, the youngest patients were patients of group 1. They showed a significant difference to the older groups regarding the means of metopic suture OES. The mean of the sphenoccipital OES showed a difference between group 3 and group 6 in MRI measurements. Also in CT measurements, there was a significant difference in the mean of the sphenoccipital OES between group 3 and 6.

4.1.4 Gender aspects

Regarding gender aspects, some studies assume no gender or racial aspects in suture width. (37) Looking at suture ossification, there are differences found that assumed males to show a more proceeded suture closure than females.(8) In this study there is a gender aspect revealed in the means of total OES and means of skull base OES points in CT measurements. The mean value of total OES points of female patients was higher than the mean value of total OES points of male patients. The female patients also showed a higher value in the mean of the skull base OES than male patients in CT measurements. (demonstrated in Figure 12, Figure 14 and described in section 3.2.4). This leads to an assumption that female patients showed more ossified measurement areas than male patients of the same age group.

4.2 Limitations

4.2.1 Patients and imaging methods

The groups in this study had different age limits, especially group 6 had a very wide age range. To estimate age at certain years of life the limit values of the age group should be closer. Multiple factors in arranging the material and methods of this study lead to a small number of patients. The number of patients was limited by exclusion criteria and the single center study design. To include more patients, further studies, eventually including other centers, are necessary. The images were provided by the data base, because it was a retrospective study. Another limiting factor was the need for high resolution images which was granted by a slice thickness of 1,5mm at maximum for CT images. These days the performance of high resolution CT scans with a slice thickness of maximally 1,5 mm is becoming more common than a few years ago. The MRI images had to be in a 1mm Flash 3D sequence to reveal the sutures and to measure them along their course.

Due to the retrospective design of the study, standard sequences and standard slice thickness of MRI images were used for measuring and scoring the sutures. In an optimized sequence with even thinner slice thickness and higher resolution the evaluation of the ossification of the cranial sutures could be more detailed and could lead to more significant results.

MRI images were used for measurement and scoring, because unlike CT there is no X-radiation exposure which is a favorable factor in applied medicine and age assessment. (3) Most scans for infants and children are taken in intubation and sedation, which could be a controversial issue when it comes to the indication of a cranial scan for age assessment only.

4.2.2 Score

The HU and signal intensity limits values were chosen by measuring tissues with similar radiological characteristics as an open, closing or ossified suture. The limit range for the objective measuring and scoring was set after defining subjectively the open, closed and ossified characteristics of the suture. The subjectivity in choosing the measuring points was a limitation of this study. There were no defined measuring points like endo-/ectocranial side or landmarks were used. Though there were 9 measuring points per suture, an even more defined area, eventually assessed by certain distance to certain anatomical structures, could lead to more objectivity.

The objective scoring was based on a point system, with a minimum of 1 point and a

maximum of 3 points for each measurement. This lead to a wide range of the definition “closing” for sutures (10-26 points), for the skull base (46-134 points), for the skull cap (37-107 points) and for the total skull (82-242 points). For a better description, the score points of a closing structure could be subdivided.

In this study only 6, of which 3 are paired, sutures were measured and scored. For a better assessment of the ossification of the skull more cranial sutures should be included in further studies.

Further statistical assessment of the measuring and scoring data could lead to a more detailed assessment of the age dependent ossification. For example, a receiver operating characteristic (ROC) analysis of the data could reveal the sensitivity and specificity of the scoring method. This would lead to predictive values and could support the age determination between adolescents (aged 14 to <18 years) and adults (aged 18 to 99 years).

4.2.3 Influences

Post maturation there is a constant degenerating of the adult skeleton. (8) This could lead to various findings of suture characteristics, because the ossification could be influenced by low bone density. The relevant comparison parameters and values of HU for CT and signal intensity for MRI images would be different and the score of this study could not be applied on those skull measurements.

For further studies, it will be important to include all varieties of skulls and their ossification patterns to reach an overview of physiological ossification of the skull and its sutures, as well as the physiological varieties. On the other hand, in this study only healthy individuals were included, but to compare these findings to disease related ossification of the sutures and to reveal the influence of these diseases on the ossification, the exclusion criteria should not include diseases or syndromes.

4.3 Conclusions

This thesis shows the possibility of revealing a relation between ossification of cranial sutures and age in humans.

To receive more quantitative results and to reach better conditions for statistical tests, more data is needed. The number of patients needs to be far higher to reach a normal distribution of the score points in each group.

The determination of age is a multifactorial approach, which needs as many indicators as are available. Age of a human individual should not ever be determined by only one factor. The grade of suture ossification can be used as an additional method of age assessment. In living it can add physical examination. In forensic examinations, the histopathological investigation can lead to microscopic findings and to a clearer description of the ossification of the cranial sutures, but they are implemented post-mortem. (8)

In forensic questions on living individuals the age assessment by evaluating the ossification of cranial sutures can be an additional factor in solving legal matters like the age of criminal responsibility or retirement age for pension claims. (70)

The CT images can be used for age determination in living humans and also post-mortem, though only living patients were included in this study. (16,19,39,65)

Optimized sequences of MRI images could be used for measuring and scoring the ossification of cranial sutures and could lead to a new method of age determination. For this purpose, further studies are needed.

As “forensic anthropology continues to be an evolving field of study, not simply an application of standard methods “(8), also the research of age determination will continue, not only for forensic aspects but also for a better knowledge about bone structures and the influences they are exposed. (9,31)

Various studies, subjective or objective, lead to a better understanding of cranial bone fusion, ossification of the sutures and aging of the skull.

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6.2 MRI data

ID	M	S						LlBex						LlBin						SO						SSBin						SSBex						OMlBex						OMlBin																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																														
		age	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																	
M2_F_01	2	2	133,833	3	75,25	3	2	157	2	2	116,5	2	2	245,75	2	2	196,5	2	2	123,25	1	2	158	2	2	100,444	2	2	161,333	2	3	95,333	3	2	158	2	2	134	2	2	215,833	2	2	203,5	2	2	145,667	2	2	149,235	2	3	94	2	2	137	2	3	93,333	2	2	129,25	2	2	117	2	2	243,333	1	2	218,25	1	2	132,167	2	2	141,444	1	3	91,556	3	2	124,25	2	2	184,833	3	3	79,75	3	2	141	1	2	157,5	2	2	189	2	2	163	2	3	70,5	2	3	88,833	2	2	132	2	2	161,5	2	2	152	2	2	122,333	2	2	206,333	2	2	126	2	2	143,833	2	3	92,444	2	2	103,333	2	2	131	2	2	160,167	2	2	159	2	2	119,167	2	2	240,5	1	2	164	3	2	112,5	1	3	82,8	3	3	96,889	2	2	215,333	2	2	106,8	3	2	121,167	2	2	148,5	1	2	178,5	3	2	136	1	2	149	3	2	168,5	1	2	239,333	2	3	96,5	3	2	103,5	3	2	137	2	2	197,5	2	2	144	2	2	124,8	2	2	127,5	2	2	163,5	2	2	234,167	2	2	118,5	2	2	115	2	3	97	3	2	255	2	2	212,333	1	3	82,9	3	3	84,875	2	2	172,7	2	3	84,75	2	2	149	2	2	142,5	2	2	160,833	2	2	150	2	2	117,5	2	2	149	2	2	137,25	2	2	138,75	2	2	107,25	2	2	185,833	2	2	127,75	2	2	162,75	2	2	148,25	2	2	104,667	2	2	168,25	2	2	123,4	2	2	230	1	3	82,5	2	2	174,75	2	2	166,5	2	2	160,25	1	2	152,75	2	2	149,5	2	2	144,75	1	2	184	2	3	79,25	3	2	269,833	2	2	145	2	2	156	2	2	157,25	2	2	117,5	2	2	109	2	2	125,75	2	3	97,5	2	3	86	3	2	232,5	2	2	191,25	2	2	161,25	2	2	144,25	2	2	111,5	2	2	134	2	2	157,5	2	3	92	3	3	76	3	2	234,5	1	2	187,5	2	2	165,25	2	2	149,75	2	2	111,5	2	2	116	3	2	167,5	2	2	121,2	2	3	49,25	3	2	137,5	2	2	173,667	2	2	169	2	2	162,5	2	2	100,75	2	2	105,5	2	2	164,75	2	3	89,75	2	2	55,25	3	2	119	2	2	155,4	2	2	164,75	2	3	95,8	3	2	127,75	2	2	167,25	2	2	114,75	2	3	32	3	2	139,25	2	2	126,25	2	2	147,5	2	2	148,333	2	2	115	3	2	105,333	2	2	135,167	2	3	67	2	3	22,167	3	3	65	3	3	25,5	3	3	27	3	2	111,25	2	3	21,25	3	2	155,5	2	3	40,25	2	3	53,25	3	3	19,25	3	3	73	3	3	21,5	3	3	17	3	2	125,75	2	3	21,75	3	2	122,75	1	3	58,5	3	3	66,5	2	3	39,2	3	3	70	2	3	25,333	3	3	21,5	2	3	11,5	2	3	18,5	3	2	106,5	3	3	48,5	3	3	61,5	2	3	29,25	3	3	32	3	3	42,5	3	3	15,5	3	2	129,167	2	3	16,75	3	3	51,167	2	3	47,333	3	3	80,75	2	3	37,75	3	3	42	3	3	19,75	3	3	18	3	2	124,75	2	3	20	3	3	24,667	2	3	49	3	3	52,833	2	3	60,75	3	3	34,25	3	3	24,75	3	3	23,25	3	2	113,667	2	3	13,8	3	3	25,5	2	3	40,667	3	3	45,5	2	3	15,4	3	3	36,25	3	3	43	2	3	55,667	3	2	130,333	2	3	23,25	3	3	20,667	3	3	17,75	2	3	61,5	3	3	20,333	3	3	53	2	3	29,25	3	3	55,5	3	2	142	2	3	15,5	3	3	27	3	3	34,667	2	3	12,75	3	3	60,25	3	3	43	3	3	37,25	3	2	144,5	2	3	9	3	16,833	3	3	31	3	3	72	2	3	89,5	3	2	158	2	2	188	2	2	215	2	1	355,833	2	2	217	2	2	133,75	2	2	164,75	2	2	188,333	2	2	55,5	3	2	168	2	2	185,25	2	2	142,5	2	1	350,5	2	2	163,25	3	2	206,5	3	2	160,8	2	2	253	2	3	92	3	2	191,5	2	2	254,75	2	2	221,5	2	1	353	2	2	192,75	3	2	153,5	2	2	146,25	3	2	260,25	1	3	46	3	2	204,5	2	2	164	2	2	201,5	2	1	361	2	2	155	2	2	168,25	3	2	160,5	2	3	77,5	3	2	203	2	2	122	2	2	246	1	2	345,75	1	2	154	3	2	188,5	2	2	118,75	3	2	169,25	2	2	51,556	3	2	176,25	2	2	181	2	1	319,167	1	1	369	1	2	137,5	2	2	216	2	2	201,75	2	2	64,75	3	2	171,75	2	2	105,25	2	2	268,25	1	2	427,5	1	2	146,6	2	2	186,25	2	2	101	2	2	157,5	3	2	72,25	3	2	175,25	2	2	116,5	2	2	233,5	2	1	458	1	2	147,667	2	2	185,5	2	2	171,25	2	2	237,6	2	2	72,75	3	2	192,25	2	2	202,5	2	1	311,5	1	1	416,5	2	2	160,25	2	2	241	2	2	171,25	2	2	35,25	3	2	147,25	2	3	94	3	2	128,5	2	2	191	2	3	66,75	3	2	221	2	2	225,25	2	1	352,5	2	3	76,5	3	2	162,5	2	3	91,75	3	2	170	2	2	225,5	2	3	88	3	2	130	2	1	304,25	2	1	565,5	1	3	64	3	2	148,75	2	3	87,5	2	2	172	2	2	181,25	2	2	121,5	2	2	186,75	2	3	67,25	2	1	311,75	1	3	19,5	3	2	163	2	2	145,5	3	2	228,25	1	2	183,5	2	2	127,25	3	2	134	2	2	213,333	2	1	345,75	2	3	51,75	3	2	181,5	1	3	45	2	2	227	2	2	149,75	2	2	150,25	3	2	124,5	2	2	195,25	2	1	321,5	2	3	56,75	3	2	207,667	1	3	61,25	3	2	158,5	1	2	154	2	3	45,75	2	2	263,25	2	2	117,333	2	1	325,75	1	2	84,5	3	2	126,25	2	3	73	3	2	157,5	2	1	304,75	2	3	54,333	3	2	164,5	3	2	220,75	2	2	253,25	2	3	66,25	3	2	123	2	2	146,75	2	2	186,25	2	2	287	1	2	132,5	2	2	163,333	2	2	225,333	1	1	352,5	1	3	73,25	3	2	146	2	2	128	3	2	229,5	2	2	195,75	2	2	102,5	2	2	125,833	3	2	236,5	1	1	303,667	2	2	53,25	3	2	152,5	2	2	107	2	3	71,75	2	2	160,5	3	2	124,5	2	2	126,5	2	2	157	2	2	184	1	3	34,25	3	2	138,333	2	2	153	2	3	62,5	2	2	132,25	2	2	151,8	2	3	97,5	2	2	152	2	2	192	1	3	60,5	3	2	155	1	2	133,75	2	3	62,75	2	2	113,75	3	2	110,75	2	2	144	1	2	143,75	2	2	113,167	2	2	69,333	3	2	146,5	2	3	98,5	2	2	133,5	2	2	145,333	3	2	133,25	2	2	127,25	2	2	125,333	1	2	144,75	2	2	40,5	3	2	110,25	2	2	152,75	1	3	95,5	2	2	140,5	2	2	120	2	2	129	2	2	133	3	2	167,25	2	2	145,3	2	2	172	1	2	100	2	3	95,5	2	2	127,6	3	2	130,5	2	2	180	2	3	94	2	2	156,75	2	2	71,8	3	2	114,25	2	2	147	2	3	78	2	2	152	2	2	176	2	2	134	2	2	137,5	2	2	43,25	3	2	156	1	2	115,25	2	2	114	2	2	152,25	2	2	134	1	2	140,75	2	2	110,5	2	2	85,333	3	2	171	1	2	145	2	2	104,75	2	2	128,25	3	3	134,75	2	2	129,5	2	2	179	2	2	119,75	2	2	26,5	3	3	70	2	3	29,667	3	3	26,5	3	3	72,25	3	3	19,75	3	3	36,25	3	3	50,75	2	3	22,75	3	3	57	3	3	27,333	3	3	33,5	2	3	70	3	3	37,2	3	3	36	3	3	53,25	2	3	27,667	3	3	60,75	2	3	27,25	3	3	41,75	2	3	45,25	2	3	25	3	3	45	3	3	54,25	2	3	26,75	3	3	64	2	3	26,333	3	3	44,75	3	3	102,833	2	3	39,5	2	3	37,5	3	3	59,25	2	3	24,25	3	3	47,75	3	3	26,5	3	3	37	2	2	102	2	3	44	2	3	48,75	2	3	24,5	3	3	45,5	3	3	30,5	3	3	38,25	3	3	72,75	3	3	45,5	2	3	27	3	3	28,5	3	3	97	2	3	26,333	3	3	32,5	3	3	24,333	2	3	34,5	3	3	80,5	2	3	25,5	3	3	81	2	3	54	2	3	55,75	2	3	20,8	3	3	37,5	3	3	35	2	3	49	2	3	83,5	2	3	26,5	3	2	106	2	3	23,5	2	3	64	3	3	11,75	3	3	39,2	3	3	41,75	2	3	43	2	3	81

ID	M	age	S			LlBex			LlBin			SO			SSBin			SSBex			OMlBex			OMlBin			
			OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	
MS_F_02	16	3	54,875	3	75,5	2	167,667	2	120,75	3	1	357,5	2	3	61,375	3	3	96,111	3	3	95,667	2	3	89	3		
		3	50	3	42,833	2	184,556	2	111,833	3	2	298,5	2	3	48,714	3	2	103,167	2	2	114	2	3	76,333	2		
		3	26,5	3	61,125	3	210,5	2	153,222	2	2	280	2	3	95,5	3	3	97	2	2	129,167	2	2	115	2		
		3	32,571	3	81,091	2	236,857	1	181,833	2	1	350	2	2	106,25	2	3	89,8	2	2	118,167	2	3	99,889	2		
		3	22	3	57,625	3	227,429	2	157,5	2	1	347,167	2	3	92,889	3	2	104,286	2	2	155	2	2	103,444	2		
		3	83,25	3	190,5	2	3	49,5	3	2	101	2	3	53	3	2	176	3	2	108	2	2	293	1	2	286,75	2
		3	52,75	3	101	2	3	39,667	3	3	57,5	2	3	81,167	3	2	120,5	2	2	104,5	2	2	238,5	2	2	294,25	2
		3	1	3	141,25	2	3	57,667	3	3	40,833	3	3	64,333	3	3	93,25	3	3	90,5	3	2	275,5	2	1	304,5	1
		3	35	3	106	2	2	123,25	2	3	38,5	3	3	92	3	3	81,75	2	3	82,5	2	2	111	2	2	178,833	2
		3	31,5	3	169	2	3	90	3	3	50,333	3	3	52,25	3	3	93	2	3	65,75	2	2	125,167	2	2	196,5	2
MS_F_03	17	3	37,167	3	227,5	2	3	96,667	2	3	71	3	3	81,833	3	3	90,5	2	3	85,25	2	2	103,75	2	2	291	1
		3	61,25	3	46,75	3	2	116	2	2	154	2	3	95,333	3	2	103	2	3	62,75	3	2	108,5	2	2	159,75	2
		3	72	3	50	3	2	133,25	2	2	120,5	2	3	76,25	3	3	74	2	2	112,75	2	2	198	2	2	117,5	2
		3	69,25	3	29	3	3	78,75	2	2	175,167	2	3	84,5	3	2	102,25	2	3	77,667	3	2	126,667	2	2	203,5	2
		3	14,167	3	46,333	2	3	61,556	2	2	149,545	2	2	194	2	3	71,833	2	2	125,167	2	2	190,333	2	2	153,75	2
		3	49,8	3	76,7	3	2	115,889	2	3	86	2	2	251	2	3	90	2	2	145,6	2	2	218,5	1	2	196,222	1
		3	74,875	3	61,167	3	3	97,625	2	3	89,429	2	2	276,75	2	3	98,333	2	2	132	2	2	188,375	2	2	190,125	2
		3	79,667	3	29,444	2	2	153,667	2	2	199,167	2	2	275,5	2	3	98,833	2	2	139,5	2	2	145	2	2	135,5	2
		3	87,143	3	86	2	2	130,333	2	2	116,333	2	1	366	1	3	98	2	2	158,333	2	2	155,5	2	2	115,75	3
		3	82,333	3	48	3	2	121,167	2	2	120,286	2	1	425,5	2	2	111,25	2	2	139	2	2	161,667	2	2	179,571	2
MS_F_04	17	3	39,25	3	107	3	2	180,111	2	3	77	3	2	292,833	2	3	92,429	2	3	113,333	2	2	178,667	2	2	185,286	2
		3	32,167	3	68,444	2	2	195	2	3	97,667	3	2	211,5	2	2	119,333	2	2	118,875	2	2	146,5	2	2	151,667	2
		3	37,333	3	81	2	2	191,5	2	2	143,25	2	2	283,5	3	3	88,167	2	2	160,5	2	2	112,75	2	2	154,625	2
		3	66	3	155,333	2	2	117,5	2	3	87	2	3	96	3	2	130	2	2	112,333	2	2	169,444	2	2	176,333	2
		3	96	3	122,667	2	2	117,143	2	3	72,857	3	3	90,5	3	2	127,833	2	2	112,75	2	2	279,333	2	2	197,5	2
		3	82,333	3	132,5	2	2	110,167	2	3	77,556	2	2	171	2	2	161,143	2	2	126,75	2	2	220,444	2	2	199,571	2
		3	77,667	3	96,875	3	2	104,5	2	3	71,833	2	3	97,75	3	2	154,75	2	2	217,5	2	2	150,167	2	3	90,286	2
		3	74,375	3	56,5	3	3	92,833	2	2	102	2	2	171,5	2	2	182,5	2	2	200,5	2	2	147,833	2	2	101,167	2
		3	71,667	3	84,286	3	2	141	2	2	106,571	2	2	113,75	3	2	195,5	2	2	224,667	2	2	174,167	2	2	108,5	2
		3	65,667	3	121,25	2	2	148,5	2	2	130,25	2	3	86,75	3	2	107,5	2	3	50,833	3	2	130,833	2	3	90,6	3
ME_M_01	71	3	25,143	3	128,778	2	2	199	2	2	104,75	2	2	117,25	2	2	119,571	2	3	87,333	3	2	132,167	2	3	82,5	3
		3	85,778	3	72,556	3	2	217	2	2	170,167	2	2	125,5	3	2	135,5	2	3	90	3	2	138,167	2	2	207,222	2
		3	21,5	3	36	3	3	39,5	3	3	82,75	2	3	32	3	3	68,25	3	3	18,25	3	3	34	3	2	179,75	2
		3	54,5	3	31	3	3	75,25	3	3	84	2	3	68	3	3	93	3	3	90,5	3	3	13	3	2	202,5	2
		3	27	3	38,75	3	3	75,75	3	3	55	2	3	88	3	3	92,5	3	3	38,25	3	3	20	3	2	155,25	2
		3	41,25	3	45	3	3	38	3	2	107	2	3	57	3	3	76,75	3	3	33,75	3	3	216	2	3	50,5	2
		3	81	3	64	3	3	50	2	2	102,75	2	3	72,5	3	3	96,5	3	3	41	3	3	83	2	3	91,25	2
		3	18,75	3	24,25	3	3	31,25	3	3	77,8	2	3	42,5	3	3	23,75	3	3	45,25	3	3	62,25	2	3	41,75	2
		3	28,667	3	9,5	3	3	36,5	2	3	42,75	3	3	89,25	3	3	43,25	3	3	69,5	3	3	86,25	2	2	117,5	2
		3	12,25	3	21,25	3	3	39,5	2	3	22,5	3	3	24,5	3	3	39	3	3	19	3	3	84,75	2	2	118,333	2
ME_M_02	53	3	12,5	3	58,25	3	3	40,5	3	3	30,5	3	3	63,5	3	3	45	3	3	30,75	3	3	38	3	2	144,75	2
		3	68,333	3	177,222	2	2	251,833	2	2	192,333	2	3	71,667	3	2	186	2	2	103,667	2	2	198,75	2	1	349,4	2
		3	57,833	3	110,333	2	2	256,5	2	2	149,714	2	3	80	3	2	225,167	2	2	165	2	2	225,222	2	2	287,5	2
		3	51,667	3	56,625	2	2	172,333	2	2	211,25	2	3	88,25	3	2	146,778	2	2	194,25	2	1	300,833	1	1	367	2
		3	47,25	3	155,875	3	1	324	2	2	151,333	2	2	293,5	2	2	238,5	2	2	128,75	2	2	229	2	1	328,75	1
		3	44,889	3	81,889	3	2	225,75	2	2	200,333	2	2	237,667	2	2	282,333	2	2	187,25	2	2	218,75	2	2	184	2
		3	45,667	3	81,667	3	2	219,2	2	2	210,556	2	2	228,5	2	2	253	1	2	147,667	2	2	257,167	2	1	310,111	1
		3	79,333	3	191,667	3	2	241,833	2	2	295,5	2	2	228,25	3	3	81,5	3	2	166	2	1	532,6	1	1	372,4	1
		3	63	3	189,286	2	2	203,167	2	2	227,333	2	2	274,167	3	2	126,5	3	2	128,25	2	1	500	1	1	325,5	1
		3	64,375	3	151,667	2	2	199,889	2	2	289,667	2	2	241,75	3	2	163,167	3	2	220,5	2	2	259,167	2	1	514,889	1
ME_M_03	52	3	46,25	3	74,5	3	2	112,25	3	3	56	3	3	54	3	2	110	3	2	148,5	2	3	88,75	3	2	174,75	2
		3	42,75	3	45	3	2	126,5	1	2	108,5	3	3	50,75	3	2	142,5	2	2	195	2	3	96	3	2	171,5	2
		3	33,75	3	26,75	3	2	191,5	2	2	127,5	2	3	76,75	3	3	90	3	2	230	2	2	163,333	2	2	172,833	2

ID	M	age	S						LlBex						LlBIn						SO						SSBIn						SSIBex						OMlBex						OMlBIn									
			OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES	OES	SIV	SES										
M6_M_07	29	3	36,25	3	270,667	2	1	717,5	1	2	242,25	2	2	290	2	1	368	1	1	381	1	1	337,5	1	1	426,25	1	3	96,5	3	82,5	3	2	145,5	2	2	226,5	2	3	55,5	3	2	157,25	3	2	204,25	2	2	176	3	2	132	2	
		3	32,6	3	49,25	3	3	51	3	2	239,5	2	3	71,75	3	2	172	2	2	159,75	2	2	109,5	2	2	138,5	2	3	61	3	49,5	3	3	77,25	3	2	260	2	3	95	3	2	144,5	3	1	304	1	2	153	2	2	127,75	2	
		3	5	3	79,75	3	2	111,333	2	2	271,25	2	3	67,5	3	1	302	1	3	77,75	2	2	137,75	1	3	89,5	3	3	5	3	79,75	3	2	115	2	2	253,25	1	3	97,5	3	2	278,75	1	2	160,5	2	1	338,25	1	2	130,25	2	
		3	66	3	57,5	3	2	158	2	2	200,25	2	3	62,5	3	2	273,75	2	3	65	3	3	66	2	2	148,25	3	3	21	3	68,5	3	2	261,5	1	1	307,75	1	2	136	2	3	80	2	2	227,5	1	2	155	2	2	245,5	1	
		3	43,5	3	11,25	3	1	393,5	1	1	327,5	1	3	36	3	2	137,5	2	1	303	1	2	146,5	2	2	276	1	3	93,167	3	22,833	3	2	250,5	2	1	404	1	3	72,5	2	2	123	2	1	372,25	1	2	168	2	1	328,5	1	
		3	90	3	100,333	3	3	26,75	2	3	41	3	3	96	3	2	114,5	2	2	133	2	2	262	2	2	193,25	2	3	86,5	3	2	118,5	3	3	22,25	2	3	65	3	3	94,25	3	3	91,5	2	2	110	2	2	267,75	2	2	124,25	2
		3	68	3	112	2	3	61	3	3	76,25	3	3	90	3	2	103,25	3	2	182,75	2	2	244,75	2	2	163,25	2	3	79,75	3	3	78,75	3	3	51	2	3	77,75	2	2	168,5	2	3	52,75	3	2	131,75	2	2	295	2	2	147,5	2
		3	85,25	3	85	3	3	16,5	2	3	29,75	3	2	183,5	2	2	102,5	2	2	110	2	2	236	2	2	132,5	2	3	74,25	3	3	87,5	2	3	66,75	3	3	56,5	3	2	221,75	2	3	89	2	2	143,25	2	2	245,5	2	1	368	1
		3	62,25	3	161,5	3	3	30,25	3	3	68	3	2	132,5	3	2	155,25	2	2	152,75	2	2	108,75	2	2	109	2	3	87,75	3	3	58,5	3	3	32,5	3	3	75,75	3	3	90,5	3	2	112,5	2	2	185	2	2	153	2	2	177,75	2
		3	64,75	3	128,5	2	3	49,5	3	3	94,75	2	2	179,5	2	2	166	2	2	196,5	2	3	85,25	2	2	185,5	2	3	69,25	3	3	56,5	3	3	16	3	3	40	3	3	86,75	3	2	194,75	2	2	153,75	2	2	236,25	2	2	188,5	1
3	37	3	72,25	3	3	29,75	3	3	82	2	3	36,5	3	2	121,5	2	2	202,75	2	2	221	1	2	276	1	3	26,5	3	3	78,75	3	3	56,25	3	3	64,75	2	3	85,25	3	2	138,5	2	2	166	2	1	334,25	1	2	174,75	1		
3	16	3	52,25	3	3	58,75	3	3	65,5	3	3	85	3	2	217,25	2	2	126,75	2	2	138,5	2	2	153,75	2	3	89,75	3	3	45	3	2	110,25	2	2	107,5	2	3	43,5	3	2	188	2	2	118,333	2	2	108	2	3	81	2		
3	10	3	58,25	3	3	25,5	3	2	120,667	2	3	53,5	3	2	259	3	2	129,833	2	2	211,25	2	2	143,25	2	3	83,833	3	3	47,75	3	2	261,5	1	3	51,25	3	3	44,5	3	2	173,5	2	2	136,75	3	1	553,5	1	2	193,833	2		
3	9,5	3	30	3	3	99,25	2	3	82,5	2	2	116,5	3	3	97,5	2	3	81,25	3	1	557	1	2	217,75	2	3	16,5	3	3	60	3	3	57	3	2	105	2	3	71,333	3	3	45,75	3	2	112,5	3	1	475	1	2	230,333	2		
3	30,5	3	36,556	3	2	254,167	2	2	215,5	2	3	73,25	3	2	134,5	2	3	94,5	2	2	178	2	2	243,333	2	3	37,333	3	3	35,333	3	2	303,333	1	2	193,667	2	2	102,25	3	2	166,857	2	3	79,25	2	2	160,875	2	2	263,667	2		
3	38,5	3	42,5	3	2	232,333	2	2	195,667	2	2	137	3	2	104,333	3	3	94,167	2	2	249,111	2	2	249,111	2	3	36,667	3	2	239,714	2	2	174,5	2	3	79,5	3	3	84	3	2	172,167	2	2	135,5	2	2	299,222	2	1	383	1		
3	30,556	3	173,333	2	2	133,167	2	3	82,5	3	3	91	3	2	168,333	2	2	126,167	2	1	406,375	1	1	406,375	1	3	49,167	3	2	145,6	2	2	137,667	2	3	74,833	3	3	70,5	3	2	159,75	2	3	72,111	3	1	311,667	1	2	169,333	2		
3	60,143	3	118,5	3	2	134	2	3	67,75	3	3	90,5	3	2	192,167	2	2	199,75	2	2	109,556	2	2	109,556	2	3	36,625	3	3	49,5	3	2	116	2	3	86,444	3	3	82	3	2	232,25	2	2	254,75	2	2	157,75	2	2	110,75	2		
3	49,429	3	89,5	3	2	110,333	2	2	114,667	3	3	79,25	3	2	268,833	2	2	233,625	2	2	139,75	2	2	260,333	2	3	68,875	3	3	15,25	3	2	136,143	2	3	69,667	3	3	73,667	3	2	237,5	2	2	125,333	2	2	232,25	2	2	182,667	2		
3	19,4	3	65,571	3	2	121	2	3	73,5	3	3	93	3	2	124,5	2	2	195,5	2	2	222,625	2	1	639,8	1	3	30	3	36,333	3	3	87,167	3	3	83,286	3	3	57,333	3	2	241,5	2	2	206,333	2	1	717,25	1	1	307,667	1			
3	7	3	32	3	3	91,5	2	3	30,667	3	3	54	3	2	158,667	2	2	214	2	2	227,167	2	1	473	1	3	58	3	3	59,5	3	2	125	2	3	66,5	3	3	71	3	2	185	2	2	281	1	3	30,5	3	2	105,5	2		
3	39,5	3	27,5	3	2	112	3	3	66,5	3	3	89,75	3	2	263	2	1	425,667	2	3	47	3	2	152	2	3	54	3	3	92,25	2	3	36	3	2	139	2	3	44,5	3	1	345	1	2	144,75	2	3	98	3	2	506,5	1		
3	28,5	3	78,75	3	3	89,25	2	2	212,25	2	3	62,25	3	2	119,5	2	2	163	2	3	79,5	3	2	249,75	1	3	23	3	3	89,75	2	2	106,25	2	2	116,5	2	3	74,5	3	2	154	2	3	88,75	3	3	44,5	3	1	305,5	1		
3	39,778	3	68,5	3	2	150,75	2	1	301,5	2	2	92,75	3	2	145	2	2	162	2	3	29,5	3	3	80,5	2	3	35,5	3	3	59,667	3	3	44,5	2	1	325,5	1	3	12	3	2	134,5	2	2	278	2	3	65,333	3					
3	32,5	3	36	3	2	230	2	1	396	1	3	96,5	3	3	87	2	2	153,5	2	2	104,25	2	2	160,5	2	3	22,6	3	3	37	3	3	71	2	3	67,5	3	3	33,75	3	2	171,5	2	3	74,75	3	2	155	2	2	133,75	2		
3	50,667	3	6	3	3	38	3	3	70,5	3	3	61	3	2	169	2	3	59,25	3	2	160,75	2	2	109	2	3	18	3	3	19,5	3	3	60,6	3	3	98,5	2	3	45,75	3	2	191,5	2	2	109,5	3	2	128	2	2	106	2		
3	38	3	27,667	3	2	146,25	2	3	89,5	2	3	39	3	3	83,25	2	2	100	2	2	119	2	3	23,75	3	3	28,667	3	3	88,25	3	3	88,5	2	3	69,333	2	3	51,75	3	3	90,5	2	2	148,5	2	2	115	2	2	3	81,5	3</	