A METHOD FOR VOLUME DETERMINATION OF THE ORBIT AND ITS CONTENTS BY HIGH RESOLUTION AXIAL TOMOGRAPHY AND QUANTITATIVE DIGITAL IMAGE ANALYSIS*

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INTRODUCTION

UNTIL THE PRESENT TIME, THERE HAS BEEN NO RELIABLE METHOD OF ACCURATELY determining orbital volume in the living state. A large number of congenital, traumatic, neoplastic, vascular, and endocrine disorders may significantly alter orbital growth. These, in turn, give rise to potentially profound changes in the bony orbital volume as well as alterations in the volume of the orbital contents. Therefore, a reliable method of determining orbital volume (bony and/or soft tissue) would be a benefit to the many disciplines interested and involved in the study and treatment of altered growth and development in this area. This thesis presents an accurate and reproducible method to determine orbital volume in vivo.

An overview of the clinical problems posed by alterations in orbital volume requires a review of previous investigations in this area as well as a reflection on the anatomy and embryology of the area.

HISTORICAL BACKGROUND

Until 1898 no definite information existed in the literature with regard to the effects of simple enucleation. Only isolated reports concerning this particular problem can be found. Merkel[1] in 1891 stated that one can find a notation in the literature that the orbit does become smaller after

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enucleation. Popow[2] in 1892 extracted the eyeball of a dog, a cat, and a pig, between 2 and 3 weeks after birth and noted 2 months later, after the death of the animals, that the anophthalmic orbit had become significantly smaller. He reported that the distance from the midline of the face to the outer border of the orbit had decreased and the cranium was asymmetric with a greater curvature on the operated side.

In 1898 the committee on excision, appointed by the Ophthalmological Society of the United Kingdom, quoted the report of Gordon Byers[3] concerning the disadvantages of simple excision of the eyeball. Among the disadvantages suggested was a faulty development of the orbit and face on the anophthalmic side when enucleation had taken place early in life. Byers reported his findings in ten cases in which the eye had been removed in childhood and in which the patients were later examined as adults. He had estimated the transverse and vertical diameters of the orbital margin on both sides by means of a compass and found no arrest of orbit development as far as the outer orbital margins were concerned. In addition, he felt that the slight differences between the orbital measurements of the operated and normal orbits were of no significance. Not satisfied with this and other reports, Thomson[4] in 1901 decided to conduct his own extensive experiment in rabbits. He was convinced that the eyeball should influence the growth of the orbit and that the introduction of a glass globe into the sclerotic should minimize growth arrest. Thomson[4] conducted his experimental studies on six rabbits which had one eye enucleated at 3 weeks of age. The manifestation of orbital underdevelopment was apparent early in the experiment and the asymmetry was striking. Linear measurements after the death of the animals showed the anophthalmic orbit smaller in nearly all directions. The orbital rim was obviously contracted and the whole orbital cavity diminished in capacity. Using the data from these experimental studies on rabbits, Thomson[4] was the first to record major orbital deformities following enucleation. He assumed that the same findings would hold true in other animals and in humans.

In a series of experimental studies with rabbits conducted between 1909 and 1921, Wessely[5] attempted to establish a correlation between the growth of the eyeball and its neighboring organs. He noticed a pronounced retardation of orbital growth after the reduction of the orbital contents by artificially producing microphthalmos and by removing the gland Harder in young rabbits. Artificially produced buphthalmos increased the orbital volume, which led to an enlarged bony orbit. In humans, Wessely was able to demonstrate roentgenologically a smaller orbit on the affected side in a young, microophthalmic patient.

Sattler[6] in 1922 commented on the change in orbital size after enucleation and observed that in his anophthalmic patients, 3 to 18 years of age, a difference between the size of the orbit was noted on x-ray in spite of the fact that a glass eye had been worn. In the same year, Heckel[7] made a brief statement to the Pittsburgh Ophthalmological Society on enucleation in infants. He remarked, that an orbital implantation following enucleation would not make any difference in the orbital development and that he himself did not favor any of the advocated procedures for implantation. Stieren,[8] on the other hand, voiced his belief (before the same society) that whether or not an implant was used made a great deal of difference in the development of the orbit.

The use of implants, if only for cosmetic reasons, called for a better understanding of the orbital changes which take place following a simple enucleation. It was soon realized that the orbital volume was the most important orbital measurement and the most difficult one to determine. In 1933, Koch and Brunetti[9] developed a new roentgenologic technique for the determination of the volume and depth of the orbit and concluded that the anophthalmic orbit was indeed smaller but that it retained the same depth as its fellow orbit.

The failure of orbital development in young patients after excision of the globe early in life was also observed and reported by Vorisek[10] in 1933 and Hartmann[11] in 1936. Luza[12] in 1938 noted in his roentgenologic studies not only underdevelopment of the anophthalmic orbit but also smaller optic canals in patients who had undergone enucleation early in life.

The first major investigation of the effect of childhood enucleation was undertaken by Taylor[13] in 1939 and included 51 patients, 3½ to 43 years of age. In children, Taylor confirmed Thomson's earlier report on the arrest of orbital growth in rabbits. The orbital underdevelopment in children measured as high as 15% compared to the ophthalmic side. The ensuing deformity was noticeable into adult life and there was conclusive evidence that enucleation before the age of 5 leads to a deficiency of the bony growth of the orbital margin. On the other hand, no manifestations of major orbital changes was apparent in cases where enucleation was performed at 9 years of age or thereafter.

Until 1940, little information was available regarding the capacity of the orbit and the size of the eye, especially in relation to general body size. Using lead pullets, Gayat[14] in 1873 was able to measure the orbital volume of a skull in a 10-year-old child. The orbital volume of the child's skull was 22 ml compared to the average volume of 29 ml measured by Gayat in adult skulls. Broca[15] in 1875 and Weiss[16] in 1890 also used lead

pellets for this measurement and reported 29.74 ml as the volume of the orbit. Adachi[17] in 1904 determined the capacity of the orbit of 92 Japanese skulls with water and recorded a range of 19 to 35 ml. P'an[18] in 1932-1933 measured the orbital capacity of 90 northern Chinese male skulls with fine sand and quoted an average of 29.3 ml for orbital capacity. Whitnall[19] in 1932 gave 29.5 ml as the volume for the orbital capacity.

Schultz[20] in 1940 reported his findings in a study of the size of the eye and the orbit in 208 primates. The orbital capacity of primates was measured with rape seeds; 450 of these round, hard seeds average 1 ml. As noted by Schultz, the capacity of the orbit is extremely difficult to measure because the orbital entrance is not represented by a single plane. However, from these studies, Schultz concluded that the relative capacity of the orbit depends largely upon body size regardless of genus, sex, or age. In addition, the collected data in his study pointed to the fact that the orbital size was dependent upon the size of the eyeball in only the most general way.

In 1945, Pfeiffer[21] gave an important report and critical analysis of a further study of the affect of enucleation on the development of the orbit. He stated that on the basis of examinations, photographs, and x-ray studies of 31 patients, the removal of an eye does indeed arrest the further development of the orbit. Pfeiffer[21] viewed the ensuing orbital contraction and the reduction of the orbital capacity as a consequence of the law of adaptation. It seems only logical that if the orbital contents are reduced, the former orbital size is not needed and the vacated space can be surrendered to the neighboring sinuses, which then become enlarged. Among the orbital changes resulting from enucleation, Pfeiffer listed a smaller orbital base and a flatness (or even convexity) of the former concave walls. This finding supported previous statements that the earlier an enucleation takes place, the smaller the orbit will become later in life. In cases where implants had been inserted, the orbits were found to be larger but still remained smaller than the fellow orbits. The orbital walls were of normal contour because the implants tend to maintain the intraorbital pressure and therefore counterbalance the process of contraction. It was further reported by Pfeiffer[21] that enucleation of the eye eventually causes a reduction of the orbital size and that following enucleation, the contraction of the optic canal becomes inevitable in adults as well as in children. The manifestation of facial asymmetry in children after enucleation was not always pronounced and reportedly, the use of an implant greatly improved the cosmetic appearance in all instances.

Changes in the volume of the orbit may take place not only as a result of enucleation, but may for instance, occur as a result of orbital fractures. In

this case, enophthalmos and diplopia often become manifest. Alexander et al[22] in 1961 pointed out that a clinical method for the determination of lost orbital volume would therefore be extremely useful, since these symptoms are relieved by the restoration of this volume. The investigators attempted to determine the variation in orbital volume not only among individuals, but also between the right and left sides, and between male and female orbits. Previous methods for the determination of this volume, based on geometric calculations and on the measurements of the orbital margin, could not produce accurate values because of the irregular shape of the orbit. The sand technique was used and orbital volumes ranging from 30.5 to 38.5 ml were found. The value for the volume of male orbits was larger than that for females. Furthermore, in 77% of the cases studied in this investigation, the right and left orbits were equal in size. A method of obtaining orbital volume by radiologic techniques could not be devised within the scope of this study.

A study by Sarnat and Shandeling[23] in 1965 of the postnatal growth of the orbit in rabbits confirms and extends earlier reports on this subject. Their report is based on findings in eight young rabbits which had their right orbits exenterated. The volumes of the left and right orbits were determined from the weight and the specific gravity of silicone impressions of the orbits. The use of impression material, in this case silicone impression rubber, was felt by these investigators to be superior to previous techniques for orbital volume determinations. In the living animals, a flatness of the orbital region became apparent soon after exenteration. In the dissected skulls the exenterated orbit was smaller than its fellow. Likewise, the orbital volumes on the exenterated side were smaller than those measured on the unoperated side. Contrary to Pfeiffer's determination,[21] Sarnat and Shandeling[23] did not find that the orbit became smaller after exenteration. Instead, they noted that the orbital size became progressively larger in animals with a larger postoperative survival period. Thus, they concluded that the exenterated orbit is not really smaller but only smaller in comparison with the unoperated orbit. It must be noted that the rabbit orbit has an incomplete bony rim and thus differs greatly from that of humans.

Howard et al,[24] in 1965 reported on orbital growth in humans after enucleation in childhood at or before the age of 12. Roentgenographic findings demonstrated a decrease in the maximal orbital height of 2.7 mm and an average decrease of orbital width of 1.5 mm. Based on these findings, the investigators suggest that enucleation in infancy is associated with only a small reduction in the size of the bony orbit. Cosmetically, this reduction was thought to be insignificant. The investigators further

stated that it is quite possible to misinterpret the true amount of retardation of orbital growth following enucleation in some patients because radiation therapy or a case of microphthalmos may also cause a reduction in the orbital size. In such cases, the decrease could be erroneously attributed to the enucleation.

It is apparent from the literature prior to 1964 that few experimental and clinical reports existed regarding enucleation and its consequences. The ensuing cosmetic deformities of this operation and a general need for a better understanding of the profound changes which occur after enucleation, especially when performed early in life, impelled Kennedy[25] to conduct further and more extensive studies in both animals and humans. His investigations into the affects of early enucleation on orbital development were on a scale much larger than had been previously attempted. A series of studies was undertaken to determine orbital changes following enucleation in rabbits, cats, and in infants and children. Immediately following enucleation, silicone spherical implants were placed in the orbits of a group of experimental cats in order to establish the degree to which the orbital development was influenced by the implant. Skull roentgenograms of 42 human patients who had undergone earlier enucleation (within the first 15 years of life), were taken and compared with roentgenograms of a control group. In this study, Kennedy[25] described the striking and typical bone changes following enucleation in rabbits, cats, and in humans. The findings in this series of experimental studies confirmed Thomson's earlier report[4] of contraction of the whole orbital rim after enucleation resembling a "pursestring" effect. The average overall decrease in orbital measurement was 12.8% in the rabbit and 26.8% in the cat. The age at the time of the enucleation appeared to be an important factor in determining the degree of orbital changes; the earlier in life the enucleation was performed, the greater were the changes in the orbit. In instances where implants had been placed in the cat orbit after enucleation, the average overall decrease in orbital measurement was 22.6% compared to 26.8% without an implant. In this study of human orbits, roentgenographic findings revealed smaller orbits on the operated side in all anophthalmic patients. The decrease amounted to as much as 15% without an implant and 8% with the use of an implant. Kennedy[25] reported the same changes in the orbital walls following enucleation as Pfeiffer[21] had done earlier, ie, contraction and irregularities of the orbital wall (the former concave walls becoming flattened and even convex due to the contraction process). The combined changes in orbital measurements after enucleation suggested a similar decrease in orbital volume. As pointed out earlier, orbital volumetric determinations are extremely diffi-

cult to carry out roentgenographically because of the irregular contours of the anophthalmic orbits. Therefore, Kennedy[25] based his approximation of the decreased orbital volume on the assumption that the orbit has the shape of a cone with an eliptical base and an average volume of 30 ml. He calculated the range in orbital volume decrease after enucleation up to 19.5% in patients with an implant and up to 27.7% without one, and estimated a possible range of these values between 35% and 50%.

The use of an orbital implant is beneficial for the developing anophthalmic orbit, as Kennedy[25] demonstrated in experimental cats and from his studies of 42 patients. He stated that regardless of the age at the time of enucleation the orbital changes at full growth seemed to be less in cases where implants have been inserted after enucleation. Kennedy further noted that x-ray therapy results in an even greater decrease in orbital measurements than that which occurs after simple enucleation. In 1970, Sarnat and Shandeling[26] published a report on the determination of the orbital volume in rabbits after different intervals of postoperative survival. The imprint method[27] was used by the investigator to determine the orbital volume in 51 young rabbits after evisceration, enucleation, and exenteration. Imprints of the orbits were made with Permalastic, a rubber base material, and the orbital volume was calculated from the net weight and specific gravity of the imprint. Sarnat and Shandeling[26] concluded that the orbit is not smaller actually, but is smaller relatively, to the unoperated orbit. Generally, there was a direct correlation between lack of intraorbital mass and lack of orbital growth.

Kennedy[28] in 1972 used the imprint method for the determination of orbital volumes in five skulls (in addition, the sand technique and linear measurements were also used). These findings, in two human pathologic skulls, one with bilateral constricted orbital rims and suspected phthisical eyes, and the other with a small contracted left orbit, probably due to congenital anophthalmos, are of great interest. A 12% decrease in the orbital depth measurement of the skull with the small contracted left orbit was noted. The orbital volume in this skull was decreased by as much as 60%, to 12 ml *vs* 30 ml in the normal skull. The average percentage decrease of the orbital entrance measurements compared to the normal right orbit was 25%. The findings in the skull of a young man with presumed phthisical eyes and bilateral constricted orbital rims revealed an average decrease of the orbital entrance measurements of only 13.3% and a 16.5% reduction in the orbital volume. In this skull, all changes were noted basically at the orbital entrance, the orbital contours appeared normal. These findings by Kennedy[28] clearly demonstrated that, with the absence of an eye or with early enucleation, greater orbital changes occur

than in the case where a phthisical eye or implant is present.

All previous studies on the effect of enucleation on orbital volume in humans have been retrospective and may, therefore, not be fully accurate. Experimental animals such as the rabbit and the cat are not the most suitable models for human comparison because of their incomplete and smaller orbits. Therefore, Apt and Isenberg[29] in 1973 decided to use sheep for their study on changes in orbital dimensions after enucleation. Sheep have closed orbits and large orbital volumes (43 ml) in addition to rapid skull maturation. This makes these animals a better model for human comparison than do cats and rabbits. Apt and Isenberg[29] conducted their experiments on five lambs between 7 and 21 days of age. The animals had their right eyes enucleated, the left eye remained intact, serving as a control. After death, the orbital volume was determined by using the imprint method developed by Sarnat.[27] The comparison of the orbital measurements revealed a 35% mean reduction of the orbital volume as compared to the control side. This reduced orbital volume is consistent with the decreased linear measurements of the enucleated orbit. This data confirmed the importance of the eye's presence for normal orbital development. The investigators recommended postponement of enucleation until after maturation whenever possible, after bony orbital growth is complete.

An investigation into orbital growth after childhood enucleation was undertaken by Osborne et al[30] with emphasis on the effect of age at the time of enucleation, the time elapsed since enucleation, and the effect of an implant. The statistical analysis of the results of this investigation confirmed earlier reports of the difference between the two orbits after unilateral enucleation in children. The reduction in orbital development was most pronounced when enucleation was performed before the age of 13 years. No additional decrease in orbital size was noted among patients who had enucleation before the age of 3 and those with enucleation between the ages of 3 and 12 years. On the other hand, enucleation after the age of 12 led, several years later, to compensatory enlargement of the periorbital paranasal sinuses. An orbital implant did not have any noticeable influence on the subsequent orbital growth, unless the enucleation was performed before the age of 3 years.

In an additional study by Kennedy[31] in 1976, bone changes in the adult anophthalmic orbit following unilateral enucleation were substantiated by roentgenographic findings. These observations supported Pfeiffer's earlier report[21] that enucleation of the adult eye also results eventually in a reduction in orbital size. The roentgenographic findings in an 83-year-old woman who underwent an enucleation at the age of 42, demonstrated

definite changes in the anophthalmic orbit 41 years later. An implant had not been inserted at the time of enucleation but a prosthesis was used following the operation. In this case, the changes in the orbital rim and the walls were striking. The linear dimensions showed an average decrease of over 10%, which probably indicates a 20% (or more) reduction of the orbital volume. The ensuing cosmetic deformities included sunken prosthesis, recessed upper lid sulcus and absence of lid fold. These cosmetic defects are presumably due to the degeneration of extraocular muscles, orbital fat atrophy, and normal senile enophthalmos. The surgical procedures for the correction of these deformities must be directed toward the restoration of the lost orbital volume. Thus, an evaluation of the orbital changes in the adult anophthalmic orbit including an accurate determination of lost orbital volume, is very important in assuring the best cosmetic surgical repair.

GROSS ANATOMY OF THE ORBIT

The orbits[19,32] are two bony structures situated between the cranium and the facial skeleton. They are separated in the midline by the interorbital space and house the eyeball and necessary nerves and muscles to insure its functioning. The orbital cavities are roughly the shape of a quadrilateral pyramid with its base, corresponding to the orbital margins, directed forward and laterally. The orbital apex is the area where the orbital walls converge. The exact placement is disputed. Classically, the optic foramen, which is the passageway for the optic nerve and the ophthalmic artery, is at the apex of the orbit, but its real location is closer to the posterior portion of the ethmoids and therefore, not at the true apex of the orbit.

The orbital contents are protected by seven bones which form the orbital cavity: the maxilla, palantine, frontal, sphenoid, zygomatic, ethmoid, and lacrimal bones. All of these bones except the lacrimal bone contribute only a part of their structure toward the formation of the orbit. The bony orbit is made up of four integral parts; the floor, the roof, and the medial and lateral walls.

The floor of the orbit is comprised mainly of the thin orbital plate of the maxilla medially, and of the orbital process of the zygomatic bone laterally. The palantine bone contributes a small portion posteriorly. The orbital floor is roughly triangular in shape, with its anterior portion being concave and its posterior portion convex. It therefore gives the orbital floor a general upward inclination and a sloping down from the medial to the lateral side. The larger portion of the orbital floor is formed by the

orbital surface of the maxilla which incorporates the infraorbital groove. This groove, in turn, converts into the infraorbital canal. The medial half of the orbital floor is weakened by this canal, which serves as a passageway for the infraorbital nerve. As a result of this weakness, it is the area most often involved in blow-out fractures.

The roof of the orbit is, for the most part, formed by the orbital plate of the frontal bone with a smaller contribution from the lesser wing of the sphenoid. It is also the floor of the anterior cranial fossa. The orbital roof is concave, triangular in shape, and often consists of brittle bone. Situated about 4 mm from the orbital margin and medial to the superorbital notch is the trochlea (the pulley of the superior oblique). The fossa for the lacrimal gland is located in the anterior and lateral portion of the roof. The superior orbital rim or margin is formed by the frontal bone. Lateral to the supraorbital notch the margin is uneven, whereas it is smooth medially.

The medial wall is distinguished from the orbital roof by fine structures and is, for the most part, formed by the very delicate lamina papyracea (orbital plate of the ethmoid). In addition, the frontal process of the maxilla, the lacrimal bone, and part of the sphenoid bone (the portion located in front and below the optic foramen), make up the medial wall of the orbit. This wall has a direct relationship to the frontal, ethmoidal, and sphenoidal sinuses. The lacrimal sac fossa can be considered a depressed part of the medial orbital wall. The lacrimal groove is formed by the lacrimal crest of the lacrimal bone posteriorly, by the maxilla bone anteriorly, and by the lacrimomaxillary suture medially. The anterior and posterior lacrimal crests join together at the hamulus of the lacrimal bone. The fact that the orbital floor and the medial wall meet at a wide angle explains the occurrence of concomitent fractures of the orbital floor and the medial wall.

The lateral wall is placed at an angle of 45° to the medial wall and is directed forward and slightly upward. It is the strongest of the four walls, and the one most exposed to injuries, even though the bone in its central portion might be quite thin. The lateral wall is composed of the orbital process of the greater wing of the sphenoid, the orbital process of the zygomatic, and the orbital process of the frontal bone. A large part of the lateral wall is separated from the orbital floor by the infraorbital fissure at the apex, and from the roof by the supraorbital fissure near the apex. This wall contains the zygomaticofacial and zygomaticotemporal canals, which in turn transmit the corresponding vessels and nerves.

The orbits are protected by the orbital rims which are formed by very thick bone in contrast to the rather thin orbital walls. The orbital rims are

formed by the frontal bone above, the zygomatic bone laterally, and by the zygomatic and maxillary bones below. The transverse orbital diameter measures approximately 40 mm at the orbital margin in adults, the vertical height is approximately 35 mm and the orbital depth measures about 45 mm.

GROWTH OF THE INTERORBITAL REGION

Whenever the need for corrective orbital surgery arises (especially in the young), selection of the most opportune time and consideration of all the factors involved in the growth of the interorbital region become crucial. However, surprisingly very little information on the growth pattern of this region exists. Nonetheless, measurements of the region have been taken on dried skulls, using various reference points. Broca[15] in 1875 found the average interorbital distance between the dacryon to be 25 mm in adults while Whitnall[19] in 1932 measured 21 mm for the distance between the lacrimal points. Hellman[33] in 1927, measuring Indian skulls, recorded an overall growth of 5.51 mm between infancy and senility, with maximal growth taking place between the ages of 9 and 14 years. Hellman also observed that midline structures of the face grow more slowly than do lateral structures. An investigation by Ford[34] in 1958 into the growth of the cranial base revealed an average growth rate of 10 mm between birth and maturity. Ford attributed this rate of growth to the pneumatization of the paranasal air sinuses. Actually, Morin et al[35] have shown that there are several forces involved in the growth and development of the interorbital region. The main part of the interorbital region is occupied by the paranasal air sinuses. This region represents the midline structures between the neurocranium and the facial skeleton. The frontal, nasal, maxillary, ethmoid, and sphenoid bones contribute to the growth and morphology of the interorbital region. The orbital changes within the period of time when growth occurs, depend in part upon the development of the cranium and facial skeleton, and in part upon the growth of the neighboring air sinuses.[32] The various processes of growth include the growth of the surrounding structures, growth of the intraorbital structures, pneumatization of the paranasal air sinuses, suture growth, and appositional growth.[35]

The expansion of the neurocranium, which follows the neural growth pattern, mostly influences the superior portion of the interorbital region. The sutures included in the process of suture growth are: frontal, frontal-ethmoid, internasal, and frontal-maxillary. Growth at the frontal suture, which is open at birth but which usually fuses by 1 year of age, increases

the width of the interorbital region and allows for growth of the cribriform plate of the ethmoid bone. The critical suture for interorbital growth is the frontal-ethmoid suture, which fuses at 2 years of age. The internasal suture, on the other hand, continues to grow until adolescence, when it eventually unites with the perpendicular plate of the ethmoid. The growth of the frontal-maxillary suture proceeds as long as the maxilla continues to increase.

The interorbital region is reconstructed and built up by appositional growth, a process which includes the laying down of new bone on one surface and reabsorption on the opposite surface. As a consequence of this appositional growth, the medial orbital wall (sharp at birth) becomes smooth, and the width of the interorbital region increases.[19]

A third force contributing to the growth of this region is the pneumatization of the paranasal air sinuses (frontal, ethmoid, maxillary, sphenoid). Schaeffer[36] has demonstrated that the ethmoid air cells are the main structures which influence the interorbital dimensions. They occupy most of the lateral nasal wall at birth, but by the age of 7 the maxillary and ethmoid air cells each occupy half of the nasal walls. At 10 years of age the anterior and posterior ethmoid air cells encroach upon the frontal and sphenoidal sinuses. The ossification of the ethmoid bone is not complete until the age of 17. The frontal sinuses develop from the anterior ethmoidal air cells and are not well defined until 6 to 12 years after birth. They continue to expand until about 50 or 60 years of age, but, by contrast, the sphenoidal air sinuses enlarge only until the age of 3. The maxillary sinuses, which are small at birth, expand between 3 and 4 years of age, with a slower growth rate thereafter until age 15.

All of these above mentioned expanding forces are counteracted by the growth of the intraorbital structures, ie, the lacrimal gland, the extraocular muscles, and the eye itself. In general, the measurements of the eye and orbit are closely correlated. All measurements in embryos with induced unilateral microphthalmia[37] reveals the orbit to be much smaller on the affected side, and the entire skull and smaller orbit demonstrate a typical and abnormal growth pattern. The orbit is proportionally too large and consequently the quantitative relationship between the eye-orbit measurements are greatly changed.

The above observations on the orbital growth pattern in chick embryos seem to indicate that the normal growth of the eye is indispensable for the normal growth of the orbit but that the eye is not the only factor governing orbital growth. Furthermore, it is generally assumed that these are not valid for chick embryos alone, but may also hold true for humans.

The growth pattern of the interorbital region has its own very distinct character. Fifty percent of the interorbital growth takes place before the age of 3 and declines thereafter; growth continues, nonetheless, beyond the age of 12 until adulthood. The mean increase of the interorbital dimension is 9.9 mm between the age of 4 months and adulthood, with a constant annual growth rate of approximately 0.5 mm.[35] The rate and the amount of growth in this region is independent of the initial size of the interorbital region is mainly due to pneumatization by the paranasal air sinuses rather than to suture growth, because the frontoethmoid suture fuses at 2 years of age. However, the rapid growth rate of the interorbital region continues until about 4 years of age, 1 or 2 years after fusion of the frontoethmoid suture, and before extensive pneumatization. In addition, as the maxilla grows, the complex nasomaxillary suture contributes further to interorbital growth. Therefore, the major factors responsible for the increase of the interorbital region are: suture growth, appositional growth, and sinus pneumatization.[35]

EMBRYOLOGY

NORMAL EMBRYONIC DEVELOPMENT

In order to understand the congenital and developmental abnormalities that may arise within the orbit, a consideration of the normal embryologic development is essential.[38,39]

The general embryologic development may be divided into three states: embryogenesis, organogenesis, and differentiation.

Embryogenesis

During the preocular first stage a transformation of the ovum (after fertilization) into the primary germ layers takes place as well as the development of the embryonic plate from groups of primordial cells. The embryonic plate consists of three distinct cell layers: the ectoderm, the mesoderm, and the entoderm. The mesoderm, a thin layer of tissues between the ectoderm and the entoderm, is made up of the paraxial mesoderm (thickened, medial portion along and beneath the neural ridges) and the visceral (lateral) mesoderm, both becoming distinguishable early in the third week of development. The eye forming material is definitely determined and arranged during the third week of embryonic life or prior to the 2.6 mm stage. Disturbing factors at this early stage of development, which affect the anterior end of the neural plate, are considered lethal, and are therefore, not compatible with life. They not only arrest the further development of the eyes but also have far reaching effects upon the brain.

Organogenesis

This second period of embryonic development is the process of organization and shifting of tissues into their predetermined positions for the purpose of construction of future organs. As far as the development of the eye is concerned, the period of organogenesis begins with the appearance of the optic pits in the anterior neural folds. They are the primitive beginning of the eye and appear at the 2.6 mm stage during the third week as a pair of shallow depressions in the anterior end of the neural tube. These grooves enlarge with the continuing closure of the neural tube to become the primary optic vesicles at about the 3.2 mm stage. The optic vesicles are directly connected to the forebrain by the optic stalks. Failure of the optic pit to form results in primary (true) anophthalmia. The arrest in development after the appearance of the optic vesicles results in secondary, ie, apparent, anophthalmia. The degeneration of the optic vesicle, on the other hand, leads to extreme microphthalmos.

Invagination of the optic vesicle during the fourth week (4 to 5 mm stage) brings about the formation of the optic cup. This transformation of the optic vesicle into the optic cup is complete by the sixth week (15 to 18 mm stage). The optic cup is composed of two ectodermal layers as a result of the invagination process. It has an open outer end and a lower opening known as the fetal or choroidal fissure. This fissure extends over the whole length of the optic cup and optic stalk, almost to the wall of the forebrain.

The basic tissues involved in the formation of the eye are the surface ectoderm, the neural ectoderm, and the paraxial mesoderm. The responsibility for the development of the bony orbit lies with the visceral and the paraxial mesoderm. The visceral mesoderm of the maxillary process gives rise to the floor and lateral wall of the orbit, while the paraxial mesoderm gives rise to the upper and inner walls of the orbit.

An arrest in the normal development at this stage (before 7 mm), preventing the complete invagination of the optic vesicle to form the optic cup, may lead to cystic dilatation and, as a result, to a congenital cystic eyeball.

BONY ORBIT

The formation of the bony orbit and the calvaria is greatly influenced by the developing brain, whereas the developing eye plays only a minor role in the shaping of the orbit according to Mann.[40] For this reason, major orbital abnormalities are connected with deformities of the brain and skull rather than with defects of the eye.

The bones of the orbit arise from the mesoderm surrounding the eye.

During the fifth and sixth week, the maxillary process grows forward to form a wedge between the paraxial mesoderm and the surface ectoderm. As a result, the eye assumes a more frontal position. The formation of the bony orbit is the result of condensation in the visceral and paraxial mesoderm. The floor and the outer walls of the orbit are formed from condensations in the visceral (maxillary) mesoderm, while the roof of the orbit is developed from the paraxial mesoderm that is part of the mesodermal capsule enveloping the brain. The inner wall of the orbit arises from the portion of the paraxial mesoderm which makes up the lateral nasal process. At about the 12 to 13 mm stage (fifth week) the mesoderm has formed a thin cone around the optic cup and the optic stalk, thereby demarcating the contour of the orbit. The formation of this cone marks the beginning of the extrinsic ocular muscles. Differentiation commences at the apex of this muscle cone in the posterior portion of the orbit and continues anteriorly in the direction of the eye. The differentiation of the sclera takes place at the same time but advances in the opposite direction. The development of the bony walls of the orbit is in full progress during the second month (30 mm stage) and their construction is quite advanced by the end of the third month. The orbital walls are well developed during the fourth month and many centers of ossification are apparent. These ossification centers begin to appear between the sixth and seventh week of embryonic life; their fusion into the component bones has taken place during the sixth and seventh month of fetal life. At first the shape of the orbit seems to be determined by the growth of the circular optic cup, thereby giving it a roundish appearance. Later on, however, the orbital contours become more and more ovoid, a process, which is based on the influence of the developing orbital contents and the maturation of the bones of the skull.[41]

ABNORMAL EMBRYONIC DEVELOPMENT

A true developmental defect may first become apparent during any of the three periods of intrauterine development, and may manifest itself in any stage of development after birth, even in senility. The underlying causative factors for the majority of craniofacial deformities are manifold; most of them are assumed to typify failure of mesodermal penetration. Mann[40] classified four main types of abnormalities according to their origin; defects which are: genetic in origin, genetically determined but environmentally produced, purely environmental in origin (nutritional, thermal, infective, or traumatic), and of unknown cause (sporadic). The majority of congenital anomalies, however, seem to be determined by more than one

factor.[42] The time of development at which the defect producing agent exerts its influence on the embryo is of utmost importance. In the earliest (germinal) period of development, when cellular differentiation is not yet underway, any interference in the normal process of development will necessarily be fatal. Defects arising during organogenesis result in gross deformities of the embryo.

Very specific anomalies occur during this period when interfering agents inflict the greatest damage. With the advancing differentiation of the fetus in later periods of development, susceptibility to these agents decreases. Consequently, the resultant defects are only minor in nature. In general, during the later phases of embryonic development, when differentiation is in its final stages, nothing more severe than growth arrest or tissue degeneration may arise. It is apparent from these observations that one and the same factor, operative at different stages of development, is capable of producing a variety of anomalies or none at all.

Congenital orbital deformities may be grouped into four major categories: primary anomalies of the brain and calvaria, primary defects of the skull (and face), abnormal development of the bony orbit, and primary defects of the eye. The last (anophthalmos, microphthalmos, and coloboma with cyst) affect orbital development to a relatively small degree. The defects of the eye generally arise from disturbances within the ectodermal components, whereas major orbital deformities appear in conjunction with anomalies of the skull and brain, since the bony orbit develops from mesodermal elements. The overall shape and form of the orbitocranial region, however, is determined by the normal development of both the eyes and the brain (skull).[43]

ANOMALIES OF THE BRAIN AND CALVARIA AFFECTING THE ORBIT

ANENCEPHALY

This type of anomaly is the most severe form of brain defect. Opinion on its cause or causes is divided. The primary factor seems to be a cerebral defect, the cause of which is believed by some investigators to be due to a blocking of the neural canal. Others are of the opinion that the cerebral defect may stem from unknown factors which are completely unrelated to neural blockage. Gross deformities as far as the orbits are concerned may be apparent in this type of extreme abnormality; the orbits are usually small and shallow, and their imperfect roofs are often quite severely affected. Anencephaly is an extreme and severe developmental degeneration of the brain and is incompatible with life.

CYCLOPIA

Cyclopia belongs to a group of anomalies termed "holoprosencephaly." These gross abnormalities of the brain, orbit, and skull are the result of serious disturbances in the cleavage of the prosencephalon. Characteristic conditions in this group are the fusion of the optic vesicles and defects of the midline structures. Craniofacial anomalies of various degrees exist in this type of malformation; all are connected with some form of hypotelorism. Without question, the most severe and lethal form of holoprosencephaly is cyclopia, an aberration where a single median eye or both eyes in contact with each other (or in different stages of fusion) are present.[40] In cyclopia there is only one single orbit and optic canal present. Other, less severe forms of holoprosencephaly include: ethmocephaly (two orbits present with hypotelorism); cebocephaly (two orbits and a rudimentary nose); arhinencephaly with median cleft lip, this is the most common type of holoprosencephaly in living children; septo-optic dysplasia (a midline anomaly characterized by hypoplasia of the optic nerves and chiasm); and trigonocephaly (close orbits and a small, triangular, pointed forehead), this condition is believed to be due primarily to the premature closure of the metopic suture.

MENINGOENCEPHALOCELE

Meningoencephalocele represents a congenital herniation of brain substance and meninges through a midline cranial defect. Three types of meningoencephalocele have been recognized, according to the substance (or substances) present in the hernial sac; meningoceles, encephaloceles, and hydroencephaloceles.

ABNORMAL DEVELOPMENT OF THE SKULL (AND FACE) INVOLVING THE ORBITS

CRANIOSTENOSIS

There is a large group with this type of abnormal development of the skull and orbits.[44] In all instances, however, the cause for the disturbances in the growth of the bones seems to be a developmental failure of the primitive mesoderm. In addition, another important cause is recognized in the premature closure (synostosis) of one or more cranial sutures. Nonetheless, the primary cause for these defects remains unknown. Several theories have been advanced by various authors. Mann[40] has classified the syndrome as a true developmental anomaly of germinal origin.

The major forms of premature synostosis of sutures are: *Oxycephaly* (tower skull): The extreme shallow orbits, caused by the forward bulging

of the posterior and lateral orbital walls, may lead to severe proptosis in this type of dyscrania. *Scaphocephaly*: Long narrow skull. *Plagiocephaly*: Slanted, asymmetric skull with close orbits. The orbit is eliptical in shape, shallow, and elevated.

The two most important syndromes of craniofacial malformation are the dysostoses of the skull, and the mandibulofacial dysostoses (involving primarily the first and second branchial arches). Various degrees of orbital deformity are apparent in both syndromes.

HYPERTELORISM

Hypertelorism manifests itself by an abnormally wide interorbital distance. This anomaly may be caused (in part) by sphenoidal enlargement, or by the arrest of growth while the orbits are still in their primitive (lateral) position. This syndrome has been classified according to its underlying causes into primary and secondary hypertelorism; with further subdivision of primary hypertelorism into the morphogenetic and embryonic type.

ABNORMAL DEVELOPMENT OF THE BONY ORBIT

Anomalies of the orbital bones are numerous and occur quite frequently. They usually represent only minor variations rather than major deformities. The most common variations are the appearance of additional bones and sutures due to abnormal ossifications; of variations in the location and number of the orbital notches and canals (due to developmental aberrations); and of defects in the orbital walls, such as lack of orbital bones, dehiscences, or a porous condition of the orbital roof (cribra-orbitalis).

Clinically, conditions which cause a decrease in orbital volume are encountered most frequently. There are both congenital and acquired forms of this perplexing problem.

DECREASED ORBITAL VOLUME (BILATERAL)

CRANIOSTENOSES

Numerous congenital and developmental disorders are known to produce changes in orbital size and configuration with encroachment on orbital volume.[45] Within this group, the variety of deformities of the head and face which are produced by the entire syndrome complex of craniostenoses, are the most striking and usually the most severe. The typical anomalies evident within this complex of cranial and craniofacial deformities are

primarily the result of premature closure of one or more sutures.

Under normal conditions, the closure of suture lines (craniostenosis) occurs simultaneously with the completion of cerebral growth and expansion. The major portion of the cerebral growth takes place in utero and during the first 2 years of life; total fusion of sutures, however, may not occur until the age of 24 years. Premature sutural closure (stenosis) causes a reduction in new bone development along the suture lines, thereby severely limiting growth of the skull at right angles to the obliterated suture. Consequently, premature sutural obliteration (synostosis) during the active period of cerebral growth leads inevitably to the development of severe deformities of the cranial vault (dyscrania). However, the complete effect of premature sutural closure is not in full evidence at birth, but becomes obvious in its entirety with the increasingly abnormal growth of the cranium. The expansion of the brain (and, therefore, the growth of the skull) is forced to shift toward the direction of the remaining open sutures, resulting in typical cranial and craniofacial deformities. Depending upon the suture or sutures involved, the resulting malformation may be (1) a characteristic deformity of the calvaria, frequently involving the orbits, (2) optic atrophy because of increased intracranial pressure, and (3) abnormal bony development (thinning and digitation).

The great variety of different types of craniostenoses and their mixed forms, together with the associated clinical manifestations, makes a simple and yet complete classification of all the variant forms of this syndrome complex difficult. Nonetheless, different classification exist in the literature, adding to the general confusion.

With reference to the suture or sutures involved in the premature fusion, a distinction (within the whole spectrum of craniofacial dysostoses) has to be made between simple premature closure of sutures (which produces very characteristic forms of dyscrania), and their more complex variants. Severe orbital deformities and ocular symptoms may be apparent to varying degrees in both groups.

SIMPLE PREMATURE CLOSURE OF SUTURES

The principal deformities manifest as a result of simple premature sutural closure are turricephaly (oxycephaly, acrocephaly), scaphocephaly, and plagiocephaly. The sutures involved in this group of simple craniosynostosis usually include the lambdoidal, sagittal, and coronal sutures. The turricephalies appear to be the most common type of simple craniosynostosis. In turricephaly, the premature closure of one of the anterior sutures forces cerebral expansion upward in the direction of the anterior fontanel-

le, producing a high, pointed (tower-shaped) head. The terms acrocephaly and oxycephaly are sometimes used synonymously with turricephaly. In acrocephaly the posterior portion of the head bulges forward as a result of the premature closures of the anterior sagittal suture, leaving a "truncated skull." In "true" oxycephaly, on the other hand, the premature closure of all the sutures causes the head to appear bullet-shaped. The turricephalies may be hereditary as well as sporadic but the latter is more common.

Sagittal synostosis (scaphocephaly) seems to be a somewhat less common form of simple craniosynostosis. Its deformities are normally quite evident at birth, ie, a long, narrow skull with a prominent forehead and bulging in the squamotemporal area. Sagittal synostosis occurs either as an inherited syndrome or sporadically. The inherited type in turn may be autosomal recessive or dominant.

Plagiocephaly (slanted head) indicates cranial and facial asymmetry associated with premature unilateral closure of various sutures, particularly the coronal suture.

The primary cause for these very typical deformities of the skull is unknown. It is commonly assumed that the underlying defect is in the mesenchymal matrix, while another theory traces the cause to a defect in fetal circulation.[40,41]

ORBITAL INVOLVEMENT

Orbital involvement in these major types of craniosynostosis may be quite extensive. The orbital malformations are often very severe despite the normal development of the eyes. As a rule, the soft tissue is not affected; the involvement rests primarily with the position and growth of the bony structures. The orbital cavities are usually extremely shallow, and therefore incapable of accommodating the globe and adnexa. The resultant proptosis (exorbitism) is one of the most obvious symptoms produced by the entire syndrome complex of craniostenosis.[46] The extreme shallowness of the orbital cavities (ie, the reduced orbital volume) is caused by the foreshortening of the orbits. The greater sphenoidal wings are displaced forward, and the sagittal axis of the orbit is decreased, producing a shorter orbit. The volume of the bony orbit is determined by the configuration of the orbital walls. The reduction in orbital volume reflects a suppression of the symmetrical expansion of the brain (due to the premature closure of at least one suture). This restriction in the growth of the calvarium may produce varying degrees of ethmoid prolapse, a vertical orbital roof, a forward distortion of the lateral orbital wall, and a lateral ballooning of the greater wing of the sphenoid toward the malar bone and

the zygomatic arch. Together, these displacements contribute to the reduction of the orbital volume, thereby forcing the globe to more forward, beyond the orbital rim. The resultant pseudoproptosis is due to the extremely shallow orbits.

The ocular symptoms are secondary to the bony malformations. They include extreme exophthalmos and (eventually) visual failure. Optic atrophy is caused either by overstretching of the optic nerve through the elevation of the brain, or by the constriction of the optic canal (due to the abnormal bone formation). However, the main factor contributing to optic atrophy is probably the prolonged increase of intracranial pressure.

VARIANTS (CRANIOFACIAL DYSOSTOSIS)

Crouzon's Disease and Apert's Syndrome

Both syndromes are generally referred to as craniofacial dysostolis, this classification does not seem to be quite specific enough, because other cranial and facial deformities are often listed with this group.

Crouzon's Disease

Characteristics of Crouzon's disease are faciostenosis and synostosis of the coronal sutures.[47] Hypoplasia of the maxilla differentiates this deformity from simple turricephaly. Crouzon's disease has a definite hereditary tendency. Nonetheless, many cases occur sporadically. Mental retardation, increased intracranial pressure (because of extensive synostosis) and severe facial malformations are typical findings in patients with Crouzon's disease. The brachycephalic head (variation between oxycephaly and scaphocephaly), which is often seen in these patients, is the result of coronal and lambdoidal synostosis.

Apert's Syndrome (acrocephalosyndactyly)

Apert's syndrome, which is a true dyscrania (oxycephaly) closely resembles Crouzon's disease. Franceschetti coined the term "pseudoCrouzon" for this syndrome.

The craniofacial deformities of Apert's syndrome are associated with symmetrical syndactyly of the extremities and with other congenital anomalies: multi-craniosynostosis with craniofacial lordosis, malformations of the cranial base, faciostenosis, and hypertelorism. Apert's syndrome, which has hereditary tendencies, is basically a relatively rare variation among the craniostenoses. The profound facial deformities which are apparent in patients with Crouzon's disease, are less severe in Apert's syndrome. The ocular involvement, on the other hand, is equal in both syndromes. Both have variant forms, but specific deformities such as

craniostenosis, exophthalmos, and malocclusion, are in evidence throughout the entire syndrome complex. Each syndrome is characterized by the recession of the frontal bone (coronal synostosis). An enlarged ethmoid resulting in orbital hypertelorism is not present in patients with Crouzon's disease, as is the case in Apert's. However, the degree of recession of the supraorbital rim is sometimes grater than the facial retrusion, which gives an increased impression of the exorbitism.

INVOLVEMENT OF THE BONY ORBIT

The deformities of the bony orbit are frequently profound in both syndromes.

The major orbital malformation is the extreme shallowness, especially in the "useful depth" of the orbit. The anatomically shallow orbit is the result of the shortened orbital roof, which in turn is due to the shortening of the anterior fossa because of coronal synostosis. The shortening of the floor of the orbit, on the other hand, is the result of the hypoplastic maxillae. This, as well as the underdevelopment of the supraorbital ridge, together with the elevation of the sphenoidal wing, causes the shallow (volumetric decreased) and displaced orbits.

The specific clinical findings apparent in patients with Crouzon's disease include extreme bilateral exophthalmos, hypertelorism, arched (parrot-beaked) nose, and retromaxillism or retrusion of the facial mass rather than the commonly referred to "mandibular prognathism."[47] The extreme proptosis rapidly becomes exorbitism, because of the marked flatness and volumetric reduction of the orbital cavities. In contrast to exophthalmos, where the protrusion of the globe is due to an increase in the orbital contents, exorbitism represents a condition where an abnormally protrusive globe is due to the underdevelopment of the orbital cavity and the volumetric decrease of the bony orbit. If the "useful depth" of the orbit is, for example, reduced by 10 mm, the reduction of the orbital volume would amount to 6 ml (about 20%), which represents the volume of the globe. In Apert's syndrome, where the severe facial deformities of Crouzon's are usually absent, the orbital involvement is equally as severe as that which is manifested in Crouzon's disease. In patients with Apert's, the orbits are markedly shallow and of a harlequin configuration. In addition, hypertelorism, asymmetric exorbitism and ptosis are other specific clinical findings. The osseous anomalies of this syndrome are those seen in oxycephaly, combined with symmetrical syndactyly of the extremities.

OCULAR INVOLVEMENT

The ocular findings of Crouzon's disease and Apert's syndrome are secondary to the cranial and craniofacial deformities, and directly related to the bony malformation of the orbits with reduced orbital volume. These anomalies include extreme proptosis (which may lead to exposure keratitis), and chronic papilledema followed by optic atrophy.[6]

Carpenter's Syndrome—Cloverlead Skull (Kleeblattschudel)

These syndromes represent variant forms of Crouzon's and Apert's syndrome. Carpenter's syndrome strongly resembles Apert's acrocephalosyndactyly. However, the osseous anomalies are less pronounced in Carpenter's acrocephalopolysyndactyly. Apert's syndrome appears to be the more severe form of acrocephalosyndactyly. The ocular changes are similar to those manifest in Apert's syndrome. They are primarily due to the markedly shallow orbits (ie, reduced volume of the bony orbits). The cloverleaf skull syndrome, on the other hand, may quite possibly represent a severe form of Crouzon's disease.

The skull is hydrocephalic (Trilobed) as a result of hypoplasia of the chondrocranium. The orbits are deformed and extremely narrow, a condition which causes severe proptosis and eventually visual loss.

MANDIBULOFACIAL DYSOSTOSES

The two most widely known syndromes of this complex are the Treacher-Collins and the Pierre Robin syndromes. Others included in the complex of mandibulofacial dysostoses are the Goldenhar and Hellermann-Streiff syndromes. The most characteristic findings in these syndormes are the very peculiar facial malformations (bird of fishlike facies), which seem to be related to defects in the first and possibly the second branchial arches.[48]

The orbits are usually shallow, and the orbital walls may often be incomplete. The harlequin shape of the orbits is the result of the deformed and depressed inferior orbital rims. The paranasal sinuses are hypoplastic, and the absence of the zygomatic arches (associated with hypoplasia of the maxillae) is (radiologically) one of the most striking features of these syndromes. The anomalies may be unilateral or bilateral, and inheritance is dominant. The ocular changes are frequently very severe. They include colobomas, microphthalmia, congenital glaucoma, esotropia, and retinal detachment.

CONGENITAL DEFORMITIES OF THE BONY ORBIT (BILATERAL)

Congenital orbital malformations with changes in orbital volume may be seen (in addition to those found in primary craniofacial disorders) in various other syndromes. Congenital bone dysplasia, for instance, may cause a reduction in the orbital volume (thereby producing proptosis) because of the thickening of the orbital walls. Furthermore, narrow and deformed orbits (with encroachment on orbital volume) are evident in patients with fibrous dysplasia, where the normal bone is replaced by fibrous tissue. On occasion, children with Albers-Schoeneberg's disease (Marble-bone disease) or osteopetrosis demonstrate a bilateral harlequin shape of the small orbits, due to the bony overgrowth of the orbits. The orbital and maxillary malformations which are manifest in osteopetrosis frequently produce extreme proptosis followed by optic atrophy.

In patients with Engelmann's disease (progressive diaphyseal dysplasia),[49] a disorder which represents a diffuse bone dysplasia, small orbits causing severe proptosis are also usually present. The reduction of the orbital cavity is secondary to the thickening of the surrounding bone. The ocular symptoms (exophthalmos, papilledema, or disc edema, and optic atrophy) are related to the sclerotic hyperostosis in the base of the skull and the calvarium, they appear to be the result of a slowly progressing stenosis of the optic canal. A hereditary transmission of Engelmann's disease is not clearly established. Some investigators consider this condition a simple mendelian recessive characteristic.

Other congenital deformities, resulting in volumetric reduction include facial and craniofacial clefts, anophthalmos (extreme microphthalmos), microphthalmos, and cyclopia (synophthalmos).

Most cranial and facial malformations are related to clefts. For a detailed description and an excellent classification of facial, craniofacial, and laterofacial clefts refer to the outstanding work done by Tessier.[48]

Anophthalmia is a relatively rare condition which is caused by various embryologic malformations. Different types of anophthalmos exist which have been classified by Mann[40] into three groups.

(1) True Anophthalmia—True (primary) anophthalmia represents the failure of the optic pit to deepen and to form the primary optic outgrowth from the forebrain at about the 2 mm stage. This type of anophthalmia is not associated with other gross abnormalities.

(2) Secondary Anophthalmos—The ocular rudiments are completely absent in secondary anophthalmia because of the total suppression or abnormal development of the whole of the forebrain. Consequently, this form of anophthalmos is connected with numerous other gross deformities.

(3) Degenerative Anophthalmos—The term degenerative or consecutive anophthalmia applies to the type of anophthalmia, where the initially formed optic outgrowth has degenerated up to the point where it finally disappears completely. Clinically, however, it is virtually impossible to distinguish between these anophthalmic conditions and extreme microphthalmia. Therefore, the term "clinical anophthalmos" is used whenever the eye "appears" to be absent. The differentiation between primary anophthalmos and extreme microphthalmos can only be made by histologic examination of serial sections of the orbit. It stands to reason that, since anophthalmos usually occurs bilaterally, the cause for this anomaly is environmental in origin. In anophthalmic patients with apparently hereditary characteristics the causative factor is most likely germinal. Primary anophthalmos is associated with a smaller but basically well formed orbital cavity. Usually, ectodermal and mesodermal tissue is in evidence in the congenital anophthalmic socket. In most cases where some type of microphthalmic eye is present the orbital deformity is normally not severe. In true anophthalmia, on the other hand, the deformities are more pronounced.

The basic problem lies with the deficient orbital growth and with a microskeletal orbit. The underdevelopment is manifested in the depression of the orbital roof and in the hypertelorism involving the medial orbital wall. The orbital walls may display a mild degree of hypoplasia and the shallow orbits have a conical shape. There is a reduction in the orbital volume in patients with primary anophthalmia because the orbital volume in the growing child is to some degree dependent on the size of the globe. With increasing age, the encroachment of the expanding paranasal air sinuses is responsible for the overall reduction in orbital growth. Anophthalmos normally occurs bilaterally. In unilateral cases, the existing eye is, as a rule, abnormal and microphthalmic, and the orbital volume is also decreased on the affected side.

MICROPHTHALMOS

The term microphthalmos generally indicates an abnormality in the size of the eye as a result of the degeneration of the primary optic vesicle. Various degrees of microphthalmos exist due to the abnormal embryologic development during the period of organogenesis. However, most are associated with a number of other congenital anomalies.[50]

Pure microphthalmos, or "nanophthalmos" (a rare condition), represents an arrest in the development of the globe after the closure of the choroidal fissure. The volume of the eye is drastically reduced while other gross congenital deformities are absent. In addition, the bony orbit is

underdeveloped and the orbital volume is reduced (with similar reduction of the soft tissue mass). Furthermore, the palpebral fissure is abnormally small (narrow) and the globe lies deep in the small orbit. The unilateral cases of pure microphthalmia the face on the affected side (and even the entire body on that side) may be undeveloped. In bilateral cases, on the other hand, the condition forms part of a general underdevelopment (dwarfism).

However, pure microphthalmia (nanophthalmos) occurs only rarely. More frequently encountered is the large group of complicated (congenital) microphthalmos, which is associated with numerous intraocular malformations (eg, coloboma with cyst, congenital cystic eyeball) or where the microphthalmos is part of a syndrome (mandibulofacial dysostosis, Treacher-Collins, and Goldenhar's syndrome).

CYCLOPIA

While anophthalmos or extreme microphthalmos are the result of failure or degeneration of the optic vesicles, cyclopia represents an extremely rare anomaly of complete fusion of the optic vesicles during organogenesis.

Synophthalmos, or partial fusion of the globes, is more commonly seen than true cyclopia. However, the orbits are obviously grossly deformed in both of these conditions. These gross deformities, which represent the defective cleavage of the prosencephalon, are frequently lethal. The cause for the total suppression of the midline structures is probably environmental rather than germinal.

DECREASED ORBITAL VOLUME (UNILATERAL)

CONGENITAL MICROPHTHALMOS

In the majority of cases microphthalmia is unilateral, but the fellow eye is frequently malformed (ie, coloboma, cystic eyeball, congenital cataract). When microphthalmia is part of a syndrome (such as mandibulofacial dysostoses) and where it is associated with other congenital deformities, it is secondary to general retardation of the overall normal development. Congenital microphthalmos is always associated with gross malformation and "underdevelopment" of the bony orbits. In patients with complicated microphthalmos, on the other hand, the orbits are usually well formed but reduced in size and volume (microorbitism). Hence, the surgeon is sometimes confronted with a very tiny orbit and socket. In addition, the eyelids may be short (one half of normal length) and atrophied, as is the case in patients with congenital anophthalmos.[51]

UNILATERAL CRANIOSTENOSIS (PLAGIOCEPHALY)

The slanting head evident in patients with plagiocephaly is produced by the unilateral closure of a coronal suture or by the combination closure of a coronal and a lambdoidal suture. The affected orbit, and in fact, the entire cranial base, is severely malformed in this type of unilateral craniostenosis. The affected orbit is elliptical in shape, shallow, and elevated. The compensatory growth of the remaining open sutures on the unaffected side produces an asymmetrical, bulged, and enlarged forehead, which increases the overall impression of the orbital displacement and the general craniofacial deformity. As a result of the shallow and malformed orbit on the side of the fused suture (or sutures) extreme exophthalmos may develop.

OVEREXPANSION OF THE PARANASAL SINUSES

ANATOMY AND DEVELOPMENT

The paranasal sinuses[35,36] are a series of very intricate cavities filled with air and lined with mucous membrane. They develop late in embryonic life (or after birth) from the nasal mucous membrane and gradually invade and pneumatize the related bones. All of the paranasal sinuses originate in the ethmoidal field of the nasal fossae and ultimately pneumatize large portions of the ethmoid, frontal, maxillary, and sphenoid bones.

Normal growth processes which are responsible for the overall growth and development are also active in the development of the paranasal sinuses. Similarly, congenital malformations and developmental anatomical abnormalities of the head and face affect the growth pattern of the paranasal sinuses as well.

Their close proximity to the orbits, as well as the thinness and fragility of the separating walls, are of clinical importance in the recognition of certain ocular and orbital symptoms. It is beyond the scope of this paper to give a full description of the anatomy and development of the paranasal sinuses. However, for our purpose, a brief review of some of the basic anatomical aspects seems to be in order.

In relation to the orbit, the paranasal sinuses are divided into two groups:

(1) The anterior group is made up of: the frontal sinus which is related to the orbital roof; the anterior ethmoid cells, which are related to the medial wall; and the maxillary antrum, which is related to the floor of the orbit.

(2) The posterior group is comprised of: the posterior ethmoid air cells and the sphenoid sinus, which are both related to the medial aspect of the orbital apex; and the palantine air cell, which is related to the orbit floor.

The maxillary sinus, which is the first to appear, is quite prominent at birth. It invades the maxillary bone (laterally) and reaches its adult size at an early age (between 3 and 4 years) then continues to grow less rapidly until about the age of 15 years.

The sphenoid sinuses appear during the fourth month of embryonic life, when ossification in this area begins. They continue to increase in size only slowly until the age of 4 years, at which time pneumatization of the sphenoid bone commences and with it the expansion of the sphenoidal sinuses in the posterior lateral aspect. In the early period of growth and expansion, the sphenoidal sinuses develop symmetrically in size and shape but are seldom symmetrical following their two periods of rapid growth; one at the age of 10 years and the other at puberty. The asymmetry may be quite striking so that, on one side, the sinus may be extremely diminutive and underdeveloped, while the sinus of the other side is enormous. The enlarged sinus frequently advances beyond its designated space, thereby invading the surrounding structures.

The ethmoid sinuses are positioned between the orbits, and comprise about ten air cells within the labyrinth of the ethmoid bone. They are separated from the orbit by a very thin plate of bone, the lamina papyraces. They are the most important structures responsible for the interorbital dimensions.

The ethmoid cells are evident during the last month of fetal life. They are still very undeveloped at birth and are divided into two primary groups, the anterior and the posterior. The anterior group may vary in the number of ethmoidal cells from 2 to 10, the posterior from 1 to 11. Cases where the ethmoidal labyrinth was made up by as few as 3 and as many as 20 cells have been reported in the literature. When a large number of cells are packed together in the ethmoidal labyrinth cells compete with each other for space. The overcrowding must necessarily lead to irregular cell contours and eventually to expansion and growth away from the ethmoidal field. The thin and fragile walls of the surrounding structures post no major resistance to the extramural expansion of the paranasal sinuses and their encroachment upon the neighboring bony structures. For instance, ethmofrontal expansions into the supraorbital plate of the frontal bone are common.

The frontal sinuses appear late after birth (at about age 1 or 2 years) and are still very small at age 7. They are asymmetrical in size and shape from the outset and gradually increase in size during childhood, developing

rapidly between 11 and 15 years of age and reaching their full adult size between 20 and 25 years of age. Some growth takes place thereafter until about age 30.

As a result of genetic and developmental problems, the abnormal growth potentials may lead to numerous variations in the anatomical development of the paranasal sinuses, so that extension of the latter may invade the orbital bones, causing a reduction in the volumetric dimensions of the orbital cavity.

Thus, there are a variety of congenital and acquired conditions that give rise to changes in orbital volume. This, in turn, produces a number of challenging clinical problems including: globe malposition, extraocular motility disturbances, and cosmetic considerations. As has been already pointed out, a myriad of disease states may give rise to changes in orbital capacity. Since these symptoms are best relieved by restoration of normal orbital volume a valid method of determining this volume in the living state is desirable. Until now, numerous techniques for determining orbital volume have been proposed. However, these studies have been performed *in vitro* after the death of the experimental animal or human patient.[4,13,23,25,26,29] Additional attempts have been made to correlate x-ray measurements with orbital volume estimations without success.[22,52,53]

With the ability to image both bone and soft tissue structures, computed tomography (CT) is capable of visualizing many of the normal and abnormal anatomical structures of the orbit.[54] The precise measurements of this radiographic technique combined with recent advances in the determination of the volume of irregular objects (volume algorithms) produce an accurate and reproducible technique for the assessment of orbital volume in the living state.

Algorithms for precise volumetric estimation of various anatomic sites have been developed. Walser and Ackerman[55] have calculated the volume of fluid-filled cerebral cavities and Heymsfield et al[56] have determined the volumes of the liver, kidney, and spleen by use of this method. Adapting this technique to the orbit now allows anyone interested in determining orbital volume *in vivo* to be able to do so.

MATERIALS AND METHODS

INSTRUMENTATION

1. General Electric 8800 CT Scanner.
2. Summagraphics Digitizing Tablet (bit pad)—for tracing CT images in an electrical field.

3. Tetronix Model #4010-1 Video Display—for programming manipulation and display.

4. Versatec Model #1100 Printer—for volume print-out.

5. Digital Equipment Computer Model #PDP 11/55—for storing the tracing information and volume display and reconstruction.

RADIOLOGIC METHOD

Multiple skulls were scanned using a General Electric 8800 CT Scanner with a scan time of 5 seconds and a slice thickness of 1.5 mm or 5 mm. For the axial sections, the skull was placed in a Caldwell position with the infraorbital line angled approximately 23° cephalad. Both a frontal and lateral tomogram were done to insure correct positioning of the skull as well as to determine the sections. The orbit was serially sectioned in the axial plane using both 1.5 mm or 5 mm stacked sections. For the coronal sections, Reid's base line, the line that joins the infraorbital point to the superior border of the external auditory meatus, was placed perpendicular to the table top. The orbit was then serially scanned using continuous 1.5 mm or 5 mm sections. A reference grid to determine measurements was obtained on each series of scans to insure accuracy and define the degree of CT image minification.

COMPUTER METHOD

1. Using extrafine transparency tracing paper, the perimetry of each orbit was outlined with a number 2 lead pencil over consecutive CT scans.

2. A central reference point was identified on each CT scan which was similarly noted on the tracing paper for future use.

3. Using a Summagraphics Digitizing Tablet output as the coordinates, the previously traced orbital images were outlined also identifying the central reference point and any point on the X coordinate.

4. The traced coordinate data was displayed on a Tetronix graphic terminal and stored.

5. The centroid of each individually traced orbital image was located by the moment method described below[57,58] (Fig 1).

6. If the centroid was located within the corresponding traced orbit, it was utilized as such. However, if the centroid was outside of the traced orbit, the operator, with computer assistance, interactively selected a point located within the orbital confines for optimum volume computation.

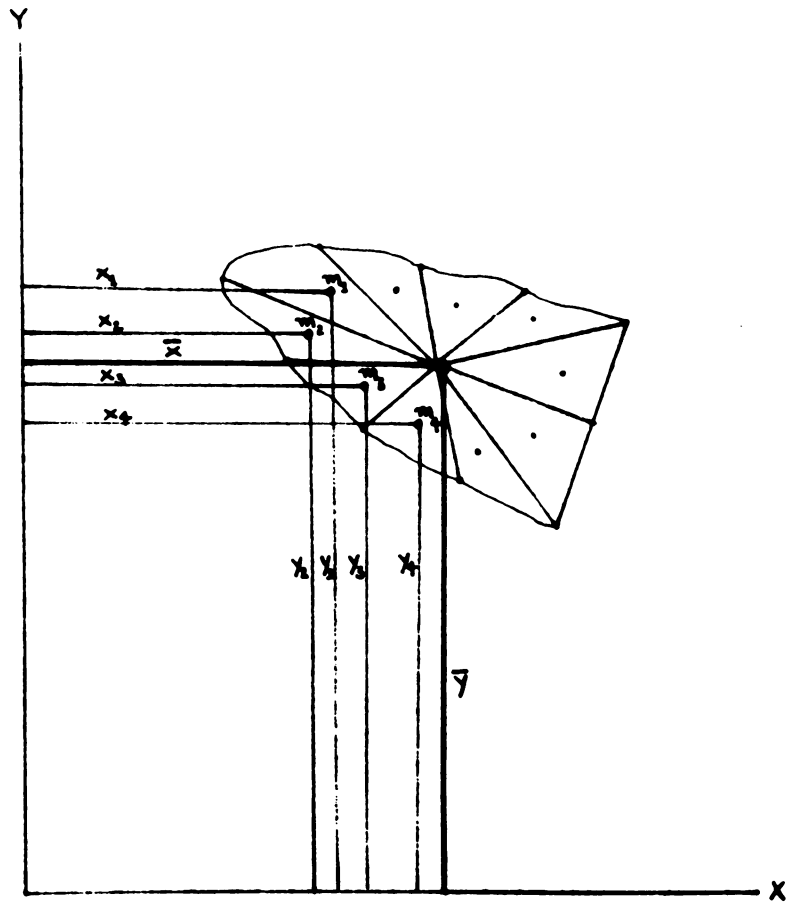


FIGURE 1
Moment method for determining the centroid of the plane

$$(\bar{x}, \bar{y}) = \left(\frac{x_1 m_1 + \ldots x_n m_n}{m_1 \quad + \ldots m_n}, \frac{y_1 m_1 + \ldots + y_n m_n}{m, \quad + \ldots + m_n} \right)$$

Where $(\bar{x},\bar{y})$ = the centroid of the entire image in one plane.

7. The surface of the orbit was approximated by polygon approximation[59,60] (Fig 2). Seventy-two sectors (or every 5°) were created around the circumference of each consecutive scan.

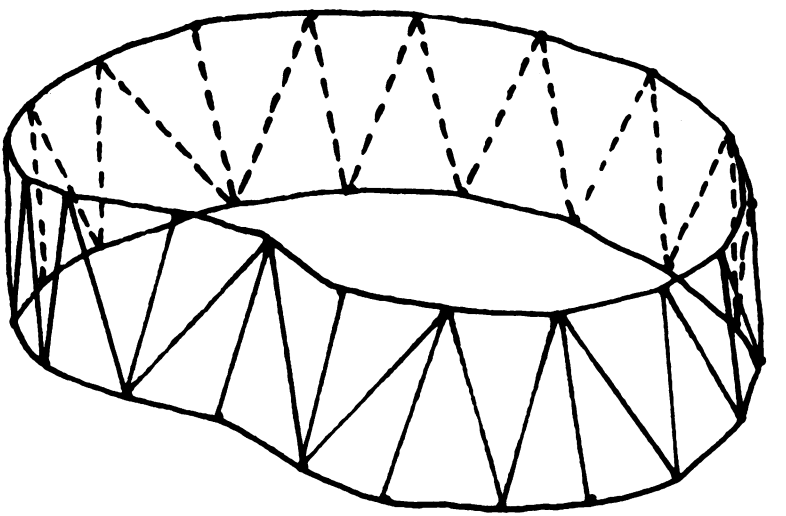


FIGURE 2
Polygon approximation—The surface between two adjacent contours using triangular tiles.

8. The volume between adjacent scans was computed by Cook's tetrahedron approximation method[61] (Figs 3 to 6). Three tetrahedrons per sector or a total of 216 (72 × 3) were created between each CT section.

9. The volumes of each individual intervening section were summated to provide the final total volume of the orbit.

10. A three dimensional orbit model generated from the traced data was reconstructed and displayed on the Tetronix graphics terminal with perspective generation[62] (Fig 7).

DIRECT METHOD

Each orbit was measured by filling it with sand according to the techniques of Alexander et al.[22] A skull was supported upright and lined with a thin sheet of cellophane. This material occupied no measurable volume. The orbit was then filled with dry sand up to the inner aspect of the orbital rim (Fig 9). This technique allowed filling of the orbit without bulging of the cellophane through the various foramina. The sand was then removed from the orbit and its volume measured in a 25 ml graduated cylinder. Ten estimations of the same orbit revealed a variation of no more than ± 0.5 ml.

Initial attempts to measure orbital volume involved measuring the amount of various materials used to fill the empty orbits, ie, lead pel-

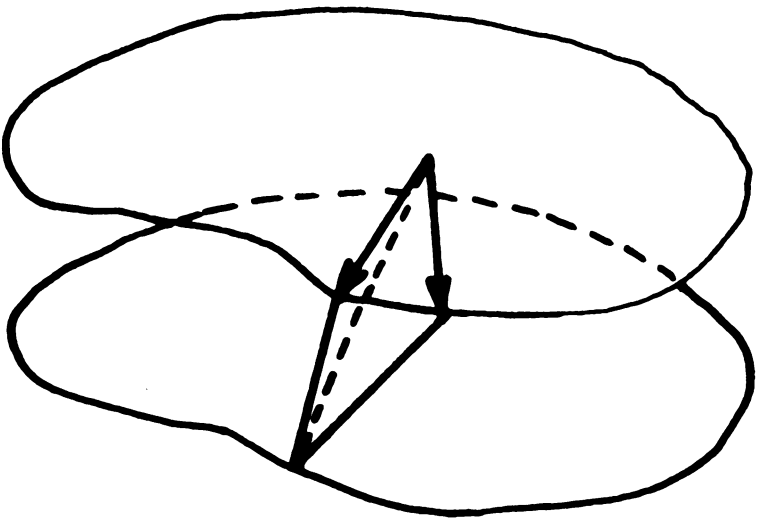


FIGURE 3
Tetrahedrom approximation—first tetrahedron.

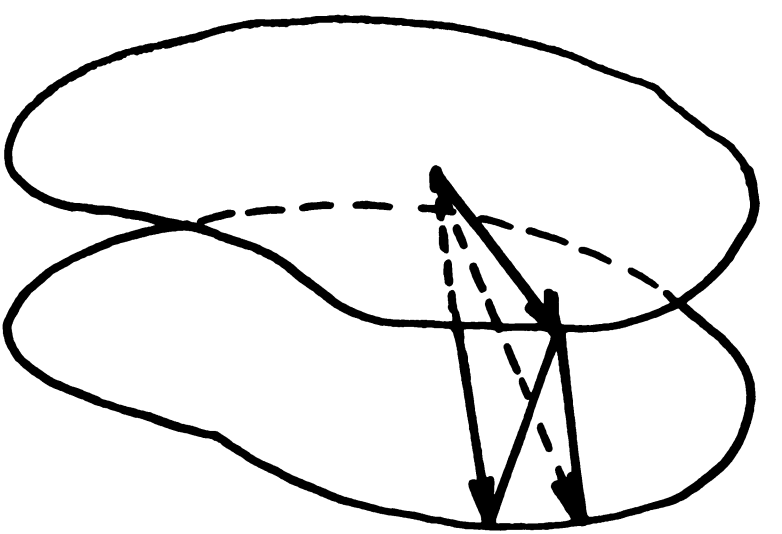


FIGURE 4
Tetrahedrom approximation—second tetrahedron.

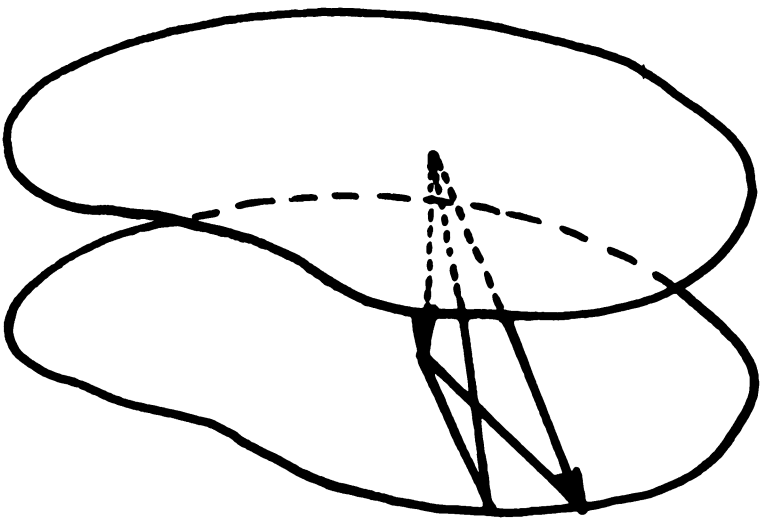


FIGURE 5
Tetrahedrom approximation—third tetrahedron.

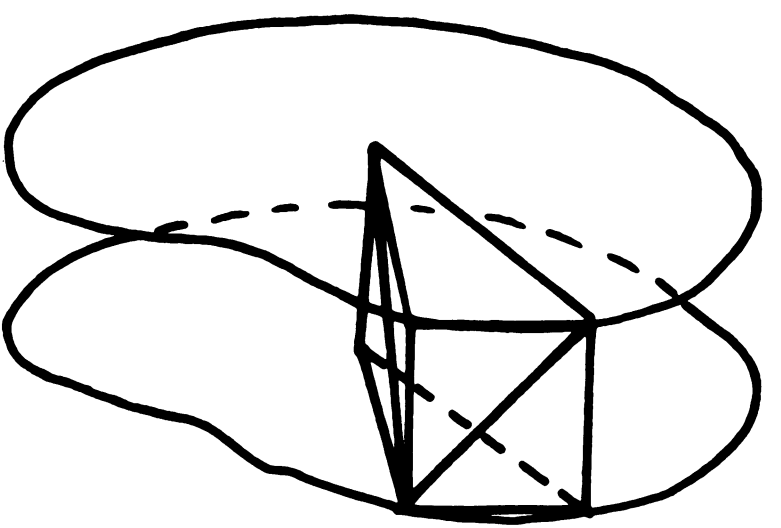
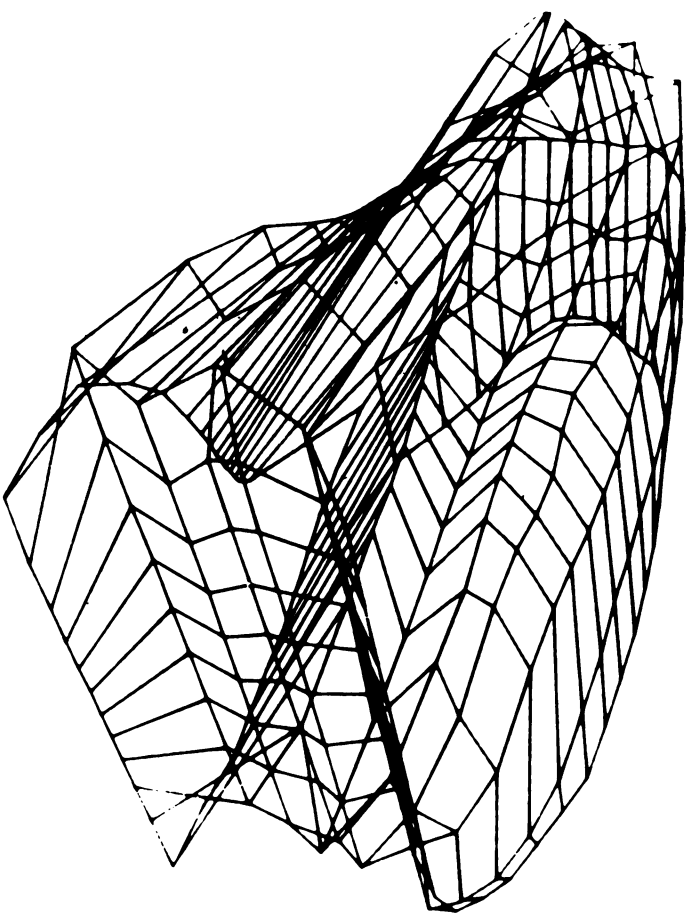


FIGURE 6
Tetrahedrom approximation composite of first, second, and third tetrahedrons.



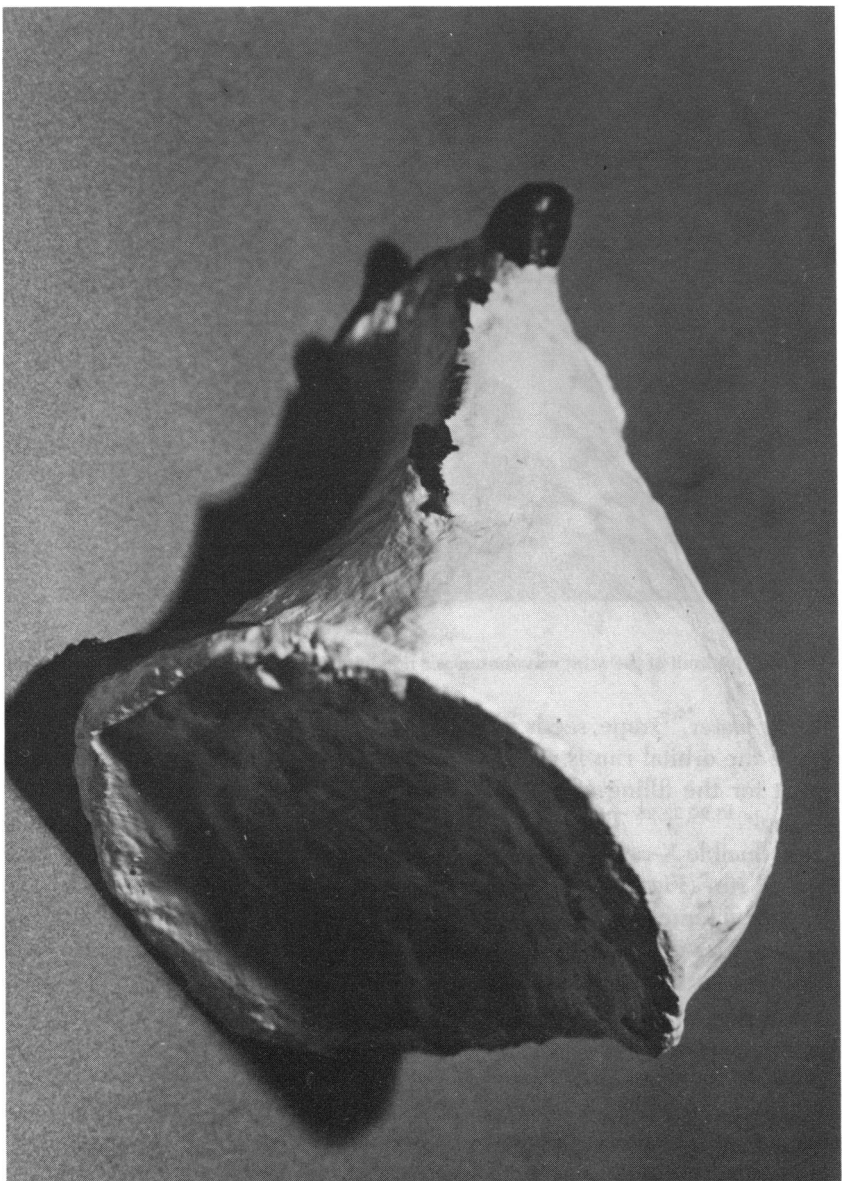


FIGURE 8
Cast of orbit. Note close comparison to computer generated orbit reconstruction seen in Fig 7.

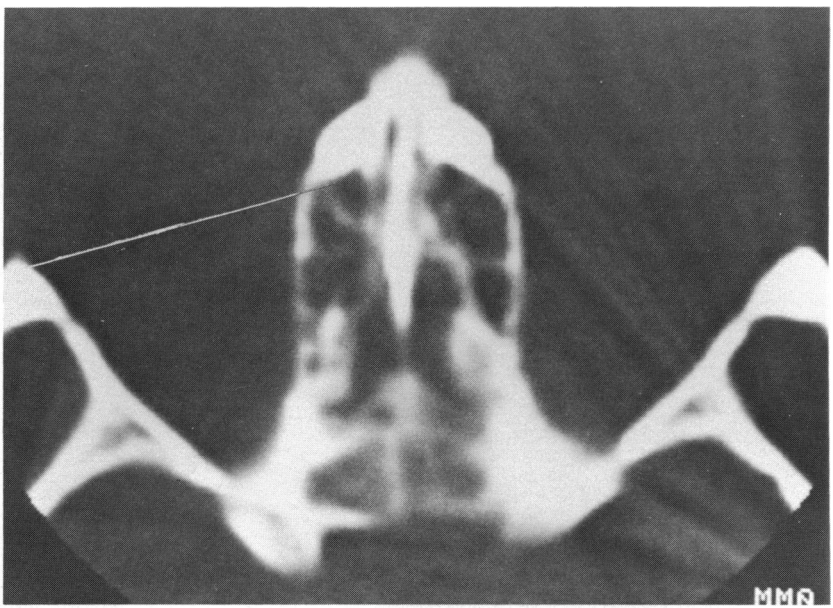


FIGURE 9
The anterior limit of the orbit was chosen as a line joining the inner aspect of the orbital rims as shown.

lets,[14] water,[17] rape seeds,[20] sand,[22] and dental impression material.[23] Since the orbital rim is not in the same plane throughout, a precise end point for the filling of the orbit by any of these materials is extremely difficult.[13,20,22,25] To circumvent this problem and to choose a readily reproducible X-ray landmark, the anterior limit of the inner aspect of the orbital rim (Fig 9) was used as the end point for the determination of orbital volume by both direct and computerized measurement techniques. This gives a volume determination somewhat less than that previously reported since the orbit is not filled to overflowing. However, since the inner aspect of the orbital rim is the last point of restraint the orbital bone structures can exert, this may be the most practical point from which to view meaningful orbital volume.

A mathematical correlation between structure and function has long been a basis for the scientific analysis of biomedical problems. Algorithms for volume estimation have been extensively utilized in biologic morphology.[63] The clinical applications of volume algorithms have been developed for a variety of organ systems with variable success.

Before the advent of high resolution CT, these efforts were limited to the use of roentgenography, ultrasonography, and radionuclide imaging.

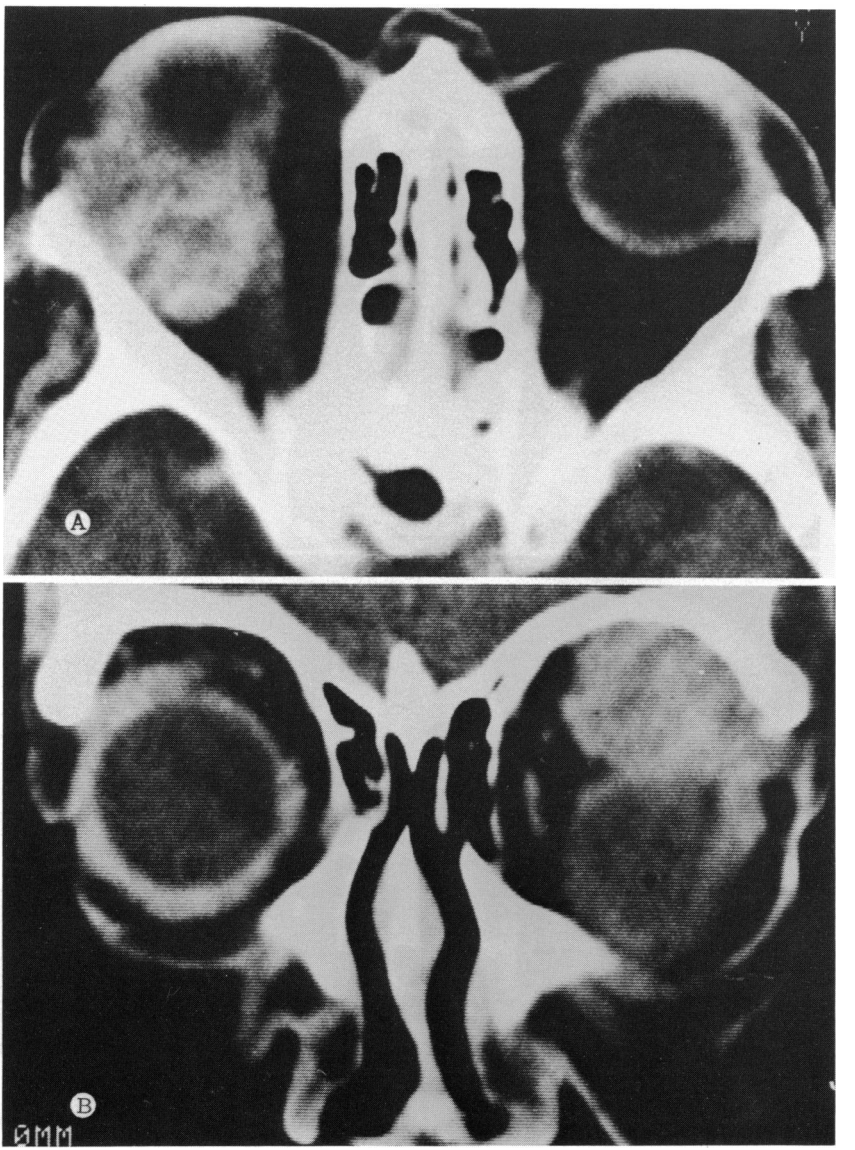


FIGURE 10

A & B: A 72-year-old woman with benign mixed tumor of lacrimal gland present for more than 15 years. Volume of affected right orbit was 24.7 ml as compared to normal left orbit with a volume of 22.0 ml. Enlarged orbit is readily appreciated in both AP (A) and coronal (B) CT sections.

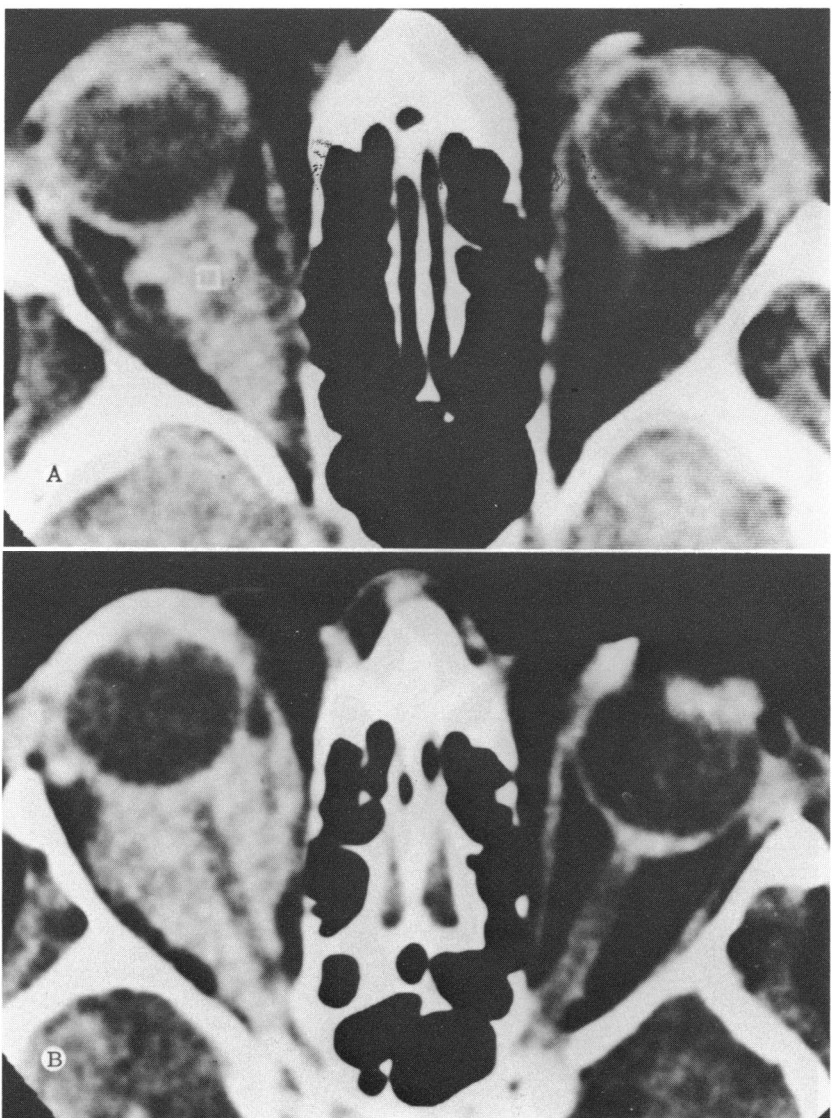


FIGURE 11

A & B: A 75-year-old woman with a right optic nerve meningioma of over 18 years' duration. These two scans are approximately 2 years apart and show a small increase in growth of both tumor and orbital volume over this period. A: Volume of involved right orbit, 24.1 ml and normal left orbit, 22.4 ml. B: Two years later, volume in right orbit, 25.7 ml and volume in left orbit, 22.5 ml.

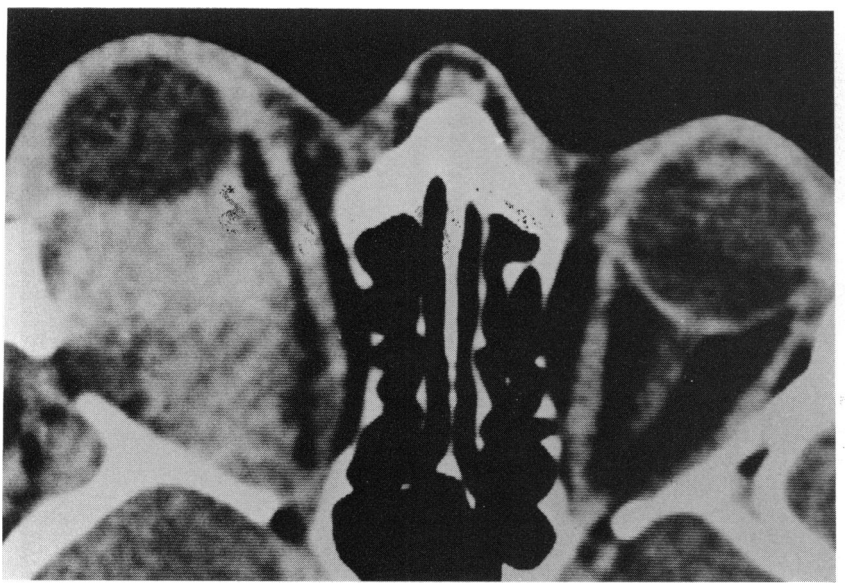


FIGURE 12
A 54-year-old man with pseudo-tumor of right orbit for more than 20 years. This slow growing, inflammatory process has caused a progressive and very substantial enlargement of right orbit over this period. Volume of normal left orbit is 23.4 ml whereas involved orbit is a full 33% larger 31.2 ml.

In many instances these methods were unsatisfactory because of interobserver variability.

As the largest organ of the body with perhaps the greatest diversity of physiologic function, the liver was probably the earliest organ system investigated for volume calculation. Roentgenographic techniques were described by Walk[64-66] and radionuclide imaging was pursued by Rollo and DeLand[67] and Eilkman et al.[68]

Volume estimates of other anatomic sites include the heart,[69-71] pituitary gland,[72] sella turcica,[73,74] and the cranial vault.[75,76] Grossly inaccurate orbital volume measurements were described by Brunetti,[10] Hartmann and Gilles,[11] and Alexander et al[22] where no volume algorithms were applied.

Reese et al[77] sought to extract quantitative measurements from CT scans via histograms and thereby laid the groundwork for volume determination as well as reconstruction algorithms.

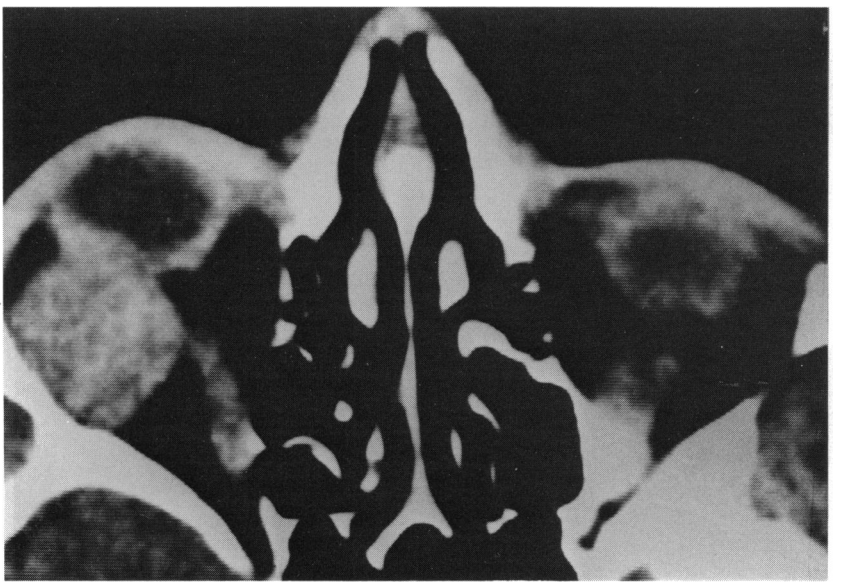


FIGURE 13
A 35-year-old woman with neurolemmoma of right orbit of 10 years' duration demonstrates a very large orbital tumor within an equally enlarged orbit. Ability of orbital volume to enlarge at a rate similar to tumor's ability to grow allows for development of virtually no compensatory exophthalmos. In this patient normal left orbit has a volume of 21.7 ml and the involved right orbit a volume of 23.7 ml.

The volume algorithm method is largely based on the acquisition of contiguous serial CT sections of the anatomic site to be studied. An accurate volume estimate can be obtained if the area of the organ as shown on each serial section is multipled by the distance between the slices.

This approach was utilized by Walser[55,78] in determining the volume of fluid-filled cerebral cavities from computed tomograms. In a similar fashion, Heymsfield et al[56] accurately measured liver, kidney, and spleen volume and mas within ± 5% error.

A number of algorithms have been developed for reconstructing a three-dimensional organ from cross-sectioned scans. Coordinate points are first acquired from the contours of the surfaces to be reconstructed, then an algorithm constructs the surfaces between adjacent contours using triangular tiles, each defined between two consecutive points on the same contour and a single point on an adjacent contour[59] (Fig 2).

The volume estimation algorithm used in this orbital study was originally developed and evaluated by Cook et al[61] who used Fuchs' method[60]

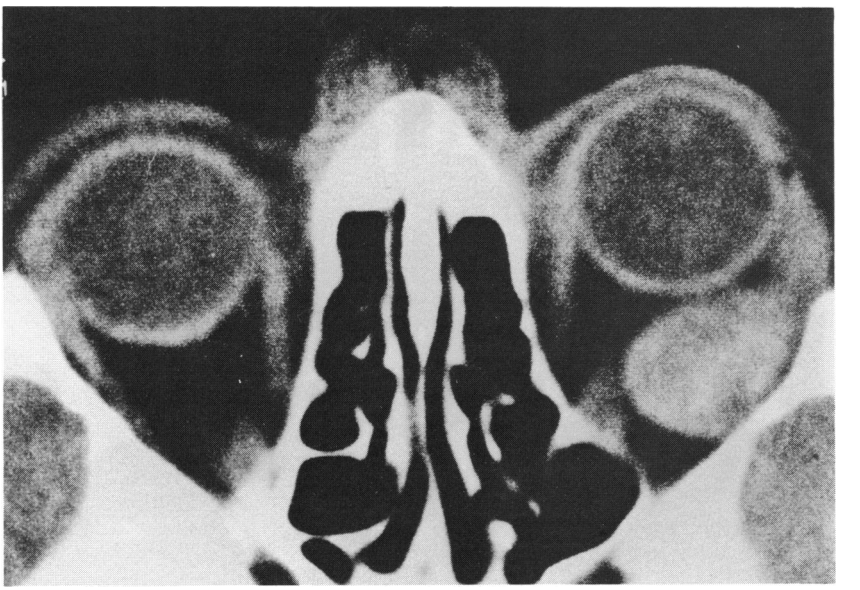


FIGURE 14
A 55-year-old man with a 30-year history of slowly developing "enlargement" of the eye. At Kronlein, a cavernous hemangioma of left orbit was removed. The left orbit increased its volume to house enlarging tumor so that very little exophthalmos was produced. Volume of normal right orbit was 22.1 ml and involved left orbit, 25.2 ml. Volume of hemangioma, 3.9 ml.

for minimizing the surface area for reconstructing the surface between continguous serial scans. If the reconstructed object was decomposed into tetrahedrons (Figs 3 to 6) the total volume could be obtained by summating the calculated volumes of the intervening spaces separating the sequential CT scans.

TABLE I: RESULTS OF DIRECT AND COMPUTED ORBITAL VOLUME DETERMINATIONS

	SKULL	CT SECTION (mm)	NO OF CT CUTS	DIRECT	COMPUTER	% DIFFERENCE
A	Right	1.5	21	22.5	23.4	4
	Left	1.5	21	23.0	22.9	0.2
B	Right	5.0	7	22.0	21.9	0.3
	Left	5.0	7	21.0	20.3	3
C	Right	5.0	8	23.1	23.5	2
	Left	5.0	5	11.5	12.0	4
D	Right	1.5	20	22.8	22.6	0.5
	Left	1.5	20	22.6	23.5	4

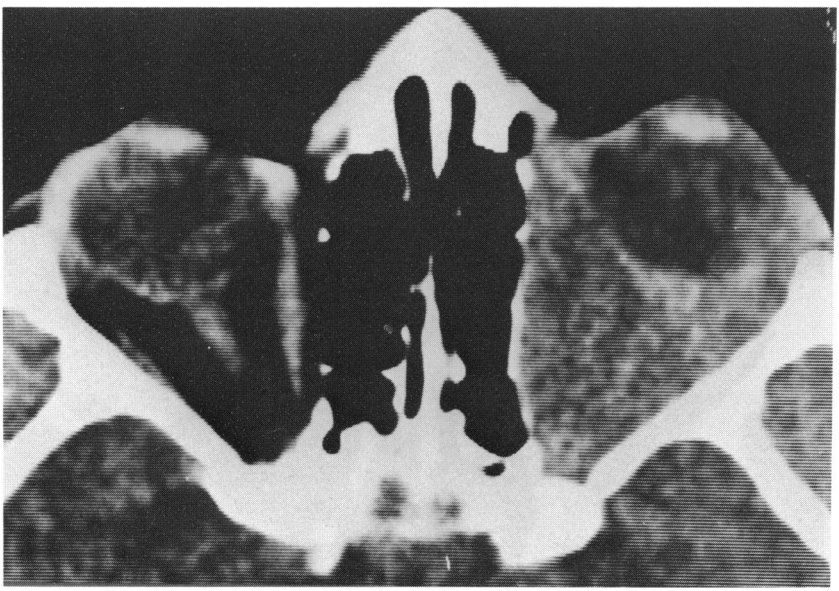


FIGURE 15
This 20-year-old woman had progressive, long-standing inflammatory disease of left orbit of many years duration. Compensatory enlargement of left orbit in this relatively young patient suggests that process began before orbital growth ceased (at about age 13 years) and prevented significant clinical exophthalmos. Volume of normal right orbit, 21.8 ml and volume of involved left orbit, 23.7 ml.

In essence then, we have taken the irregular piriform shaped orbit, serially sectioned it in its entirety with CT, decomposed its surface into polygons, its substance into tetrahedrons and thus created, with computer assistance, a form that obeys geometric formulas as we know them.

The purpose of this work is to establish the reliability and reproducibility of this technique for determining orbital volume in the living state. Accordingly, a relatively small number of orbits[8] were thoroughly studied and the results appear in Table I. Skulls A and D were measured with 1.5 mm CT "slices" from the bottom of the orbit to the top. For the most precise determinations, the first CT section must just graze the lowermost portion of the orbit and the last section must just graze the uppermost part of the orbit. This group of measurements produced, in effect, a "sandwich" of "slices" from the bottom of the orbit to the top. Each "slice" is precisely traced onto the digitizing tablet, then enters the computer. The volume of each "slice" between each CT scan is then computed by

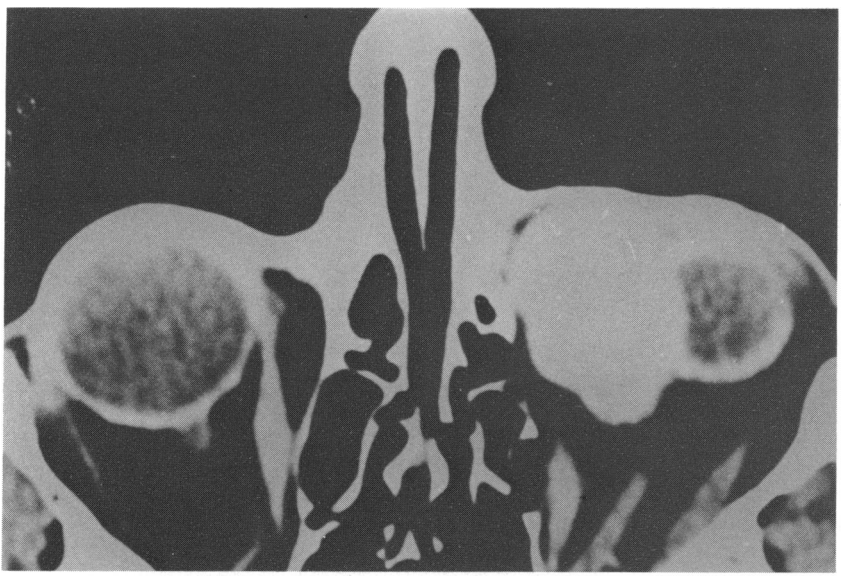


FIGURE 16
A 65-year-old man with a cavernous hemangioma of over 25 years duration. Enlarged, adaptive orbital changes prevented development of significant exophthalmos. Volume of normal right orbit, 22.2 ml and volume of involved left orbit, 24.9 ml.

Cook's tetrahedron approximation method[61] as described above. Finally, the volumes of each individual "slice" are summated to produce the total orbital volume. The skulls (A & D) measured with the 1.5 mm "slices" required 21 and 20 cuts, respectively. On the other hand, skulls B and C were measured with 5 mm "slices" and then required 7 to 8 cuts to determine the orbital volume. The left orbit of skull C is a very special case and will be discussed separately.

In addition to the computerized orbital volumes, all the orbits were measured directly by the same technique as reported by Alexander et al.[22] The only difference was the selection of the end point. As mentioned above, the anterior limit of the inner aspect of the orbital rim was used as the most forward extreme of the orbit for both computed and direct measurements (Fig 9).

Table I compares the results of the direct and computed measurements of the volumes of the eight orbits studied. The percent differences between the two methods range from 0.2% to 4%. In four orbits (A right, C

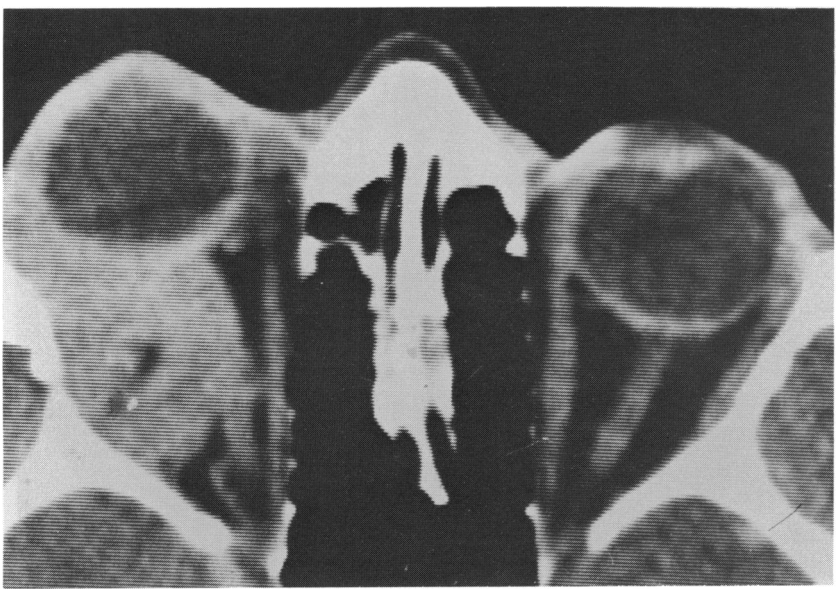


FIGURE 17
A 29-year-old woman with a long-standing lymphangioma of right orbit. Volume of normal left orbit, 21.4 ml and volume of involved right orbit, 23.5 ml.

right and left, D left) the computed volume was higher than the direct calculation (0.9 ml, 0.4 ml, 0.5 ml, 0.9 ml) whereas in the other four orbits (A left, B right and left, D right) the computed volume was lower than the direct (0.1 ml, 0.1 ml, 0.7 ml, 0.2 ml). The accuracy and reproducibility were essentially the same whether 1.5 mm "slices" were made (skulls A and D) or whether 5 mm "slices" were made (skulls B and C). Since fewer CT cuts are required with the 5 mm technique it is suggested that this be used. Multiple determinations of both the direct and computed measurements were made. The direct measurements were each repeated ten times and were reproduced ± 0.5 ml. The computed measurements represent an average of five separate determinations and were reproduced ± 0.3 ml.

The ability to study skull C represents a unique opportunity. This skull (and two of the others) was loaned to me by Robert E. Kennedy, MD and was the subject of an extensive study by Kennedy.[28] In that study orbital volume determinations were conducted by the sand and imprint methods. The volume of the normal right orbit was 30 ml and of the constricted

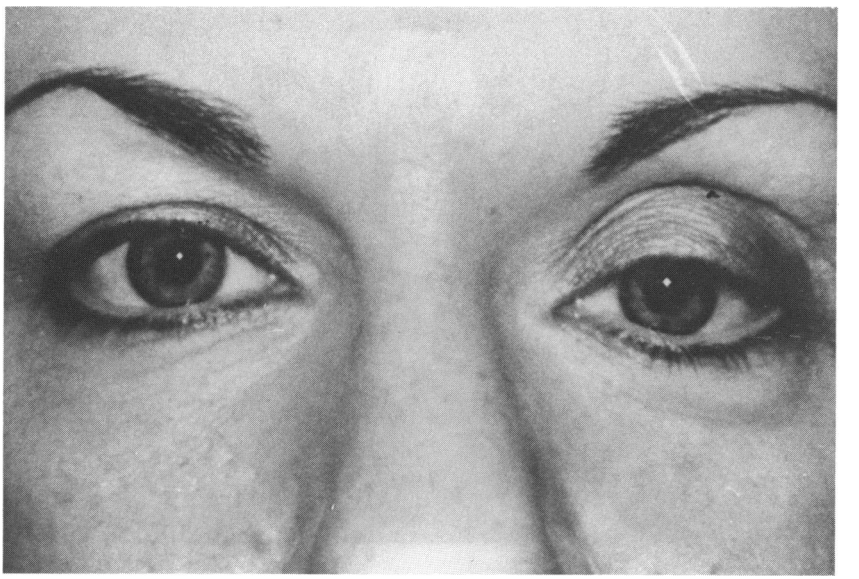


FIGURE 18
Left globe is 4 mm lower than right and 3 mm of left enophthalmos is present. (For history see text.)

left orbit 12 ml. In the current study, taking the inner aspect of the orbital rim as the end point, the direct volume measurement of the normal right orbit was 23.1 ml and the computed volume 23.5 ml. The difference reflects the end point chosen for the determination of the anterior limit of the orbit. The direct measurement of the constricted left orbit was 11.5 ml whereas the computed measurement was 12.0 ml (exactly the same as reported by Kennedy). These measurements are nearly the same in the two studies because of the bony changes in the constricted orbit. These changes modified the orbital rim so that it became flattened and there was no slope backward as is present in normal orbits. Consequently, the direct and computed measurements of this study were essentially the same as those reported by Kennedy.[28]

DISCUSSION

The ability to accurately assess orbital volume in the living state has a number of potentially useful applications.

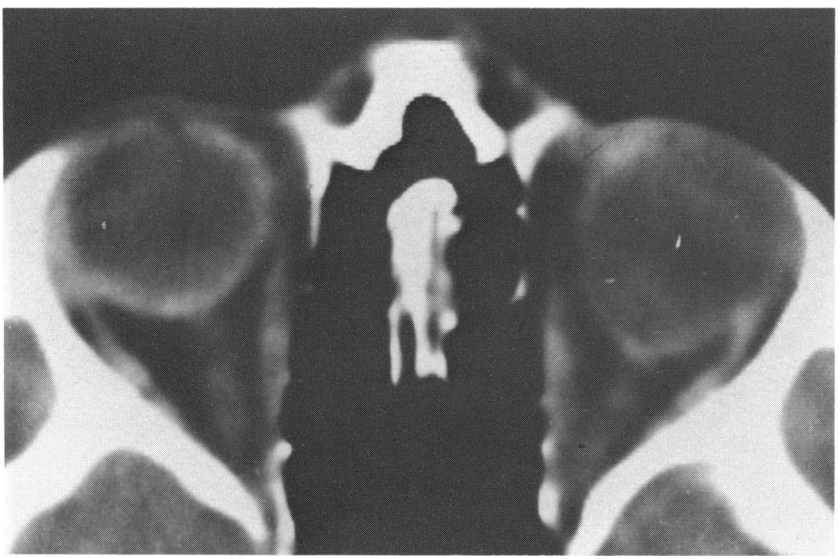


FIGURE 19
Volume of normal right orbit, 22.3 ml and volume of involved left orbit, 25.2 ml.

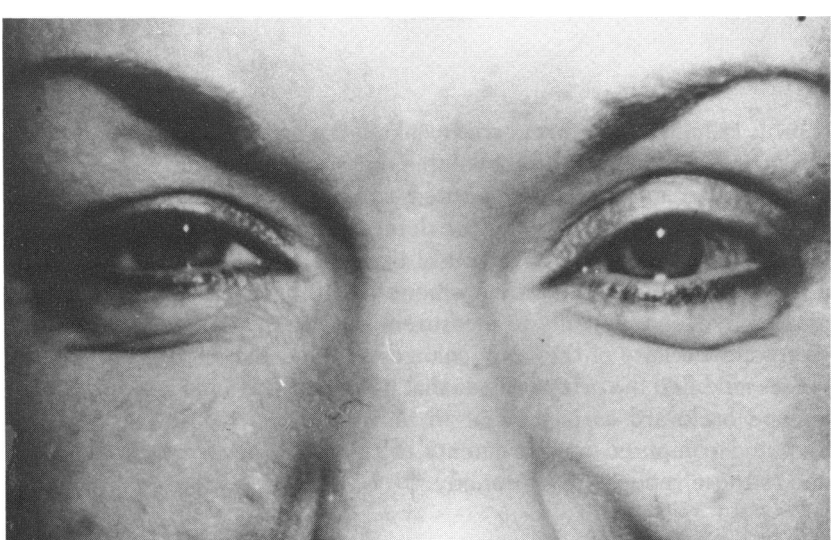


FIGURE 20
After subperiosteal insertion of 3.8 ml of silicone, left orbital volume is restored and globe ptosis and enophthalmos are corrected.

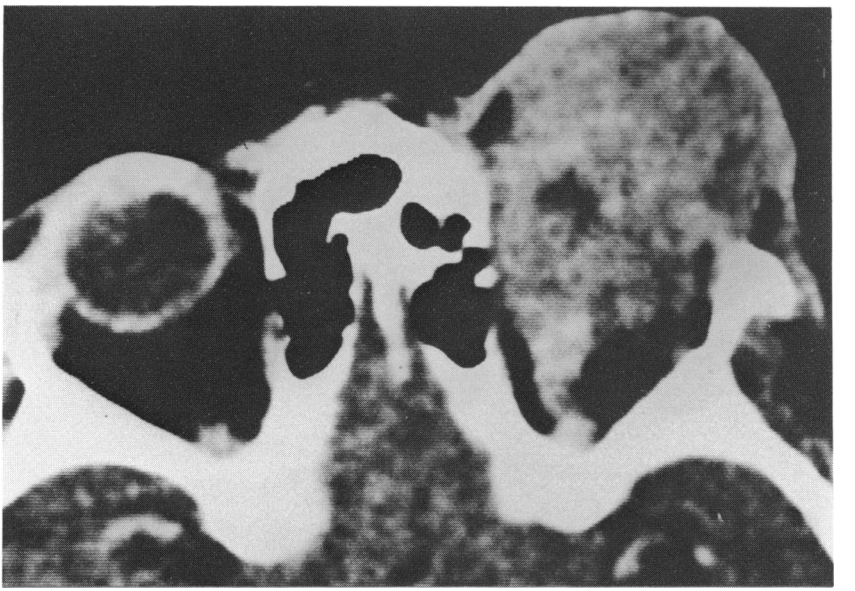


FIGURE 21
An 88-year-old woman with malignant melanoma of left orbit. There is a very large orbital tumor with no orbital enlargement because of short time during which tumor grew. Volume of normal right orbit, 21.4 ml and volume of involved left orbit, 21.6 ml.

1. Study of the orbit and its contents during growth and development.

Until now, no means has been available to accurately measure the growth and development of the unmolested orbit in experimental animals or humans. Consequently, the factors responsible for normal growth and development in this area are largely speculative.

2. Study and treatment of congenitally malformed orbits.

The problems associated with the premature closure of the cranial sutures and the craniofacial dysostoses has been discussed previously.[40-48] Tessier[48] has developed an elaborate treatment complex for many of these unfortunate patients without the capability of pre- or postoperative orbital volume assessment. Accurate measurements of orbital capacity before surgery should make the surgical planning more predictable. Postoperative follow-up of these patients would be more complete with the ability to monitor orbital volume.

3. Study and treatment of the anophthalmic orbit.

The difficulties presented by orbital volume disorders are best represented by the problems associated with the anophthalmic orbit. There is

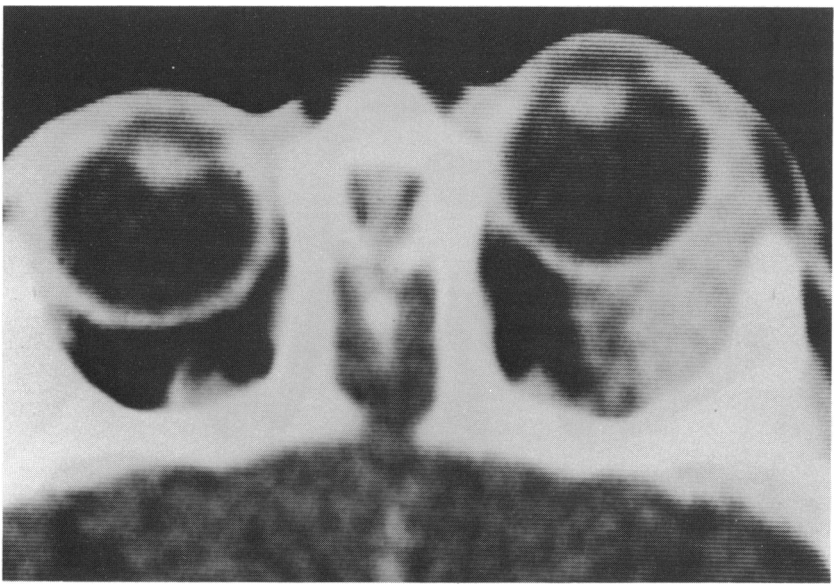


FIGURE 22
A 2-month-old girl with capillary hemangioma of left orbit. This CT scan reveals a very large orbit in a very young infant demonstrating that substantial orbital enlargement can occur over very short periods of time when intraorbital pressure elevates in neonatal period. Volume of normal right orbit, 14.3 ml and volume of involved left orbit, 17.2 ml.

general agreement that enucleation early in life results in definite bony and soft tissue changes in the orbit on the side of the surgical excision.[3-37] Studies of the human anophthalmic orbit demonstrate the substantial volumetric decrease as a consequence of orbital underdevelopment following enucleation in infancy and childhool.[4,5,13,21,25,28,30] The reduction in orbital volume may range from 20% in patients who had received an orbital implant at the time of enucleation to about 30% in patients without an implant. In the congenital anophthalmic orbit, however, the decrease in orbital volume is reportedly much higher; the reduction is about 50% and may even be as high as 60% or more in some cases. The reduction of the orbital entrance measurements in congenital anophthalmic patients amounts to 25%, whereas the depth of the orbit may be reduced by as much as 12%. In view of the magnitude of the volumetric decrease in the anophthalmic orbit, *in vivo* volumetric measurements would be of great value for better understanding and management of the enucleated orbit.

The degree of orbital underdevelopment appears to be most pronounced in cases where an enucleation was performed prior to the age of

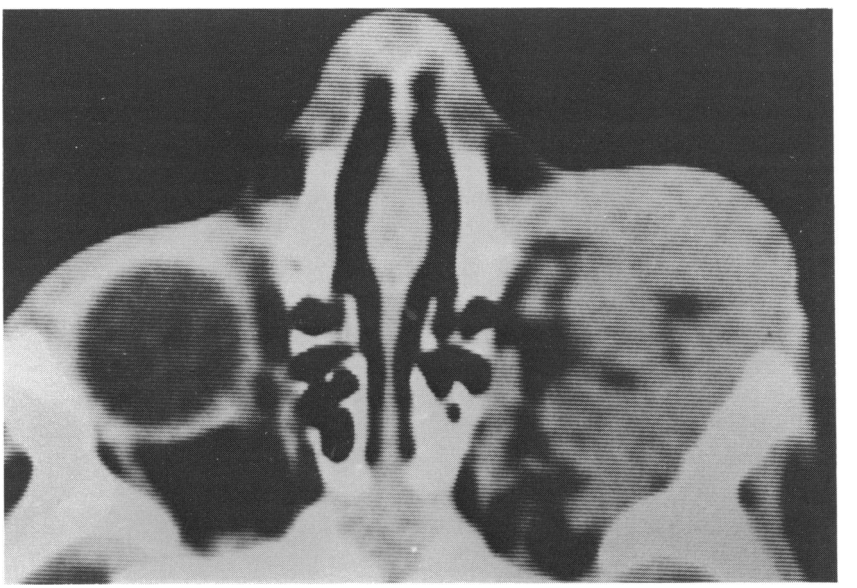


FIGURE 23
A 4-month-old girl with a capillary hemangioma of left orbit. Similar changes to those seen in Fig 23. Volume of of normal right orbit, 15.2 ml and volume of involved left orbit, 17.9 ml.

13 years. On the other hand, in patients who had an eye enucleated later than 13 years, there seems to be some, but not a significant, change in the orbital size. However, in adult life, the difference in the size of the normal and enucleated orbit may be considerable.[21,31] This long period of delay in the underdevelopment of the enucleated orbit may be explained by the fact that by the age of 13 years skull growth has slowed down to a point where it is virtually complete. The subsequent enlargement and the compensatory growth of the paranasal sinuses after enucleation, and their encroachment on the orbital cavity, takes place only gradually and very slowly.[29]

The beneficial influence of an implant on the overall development of the enucleated orbital cavity is generally recognized.[79-84] The presence of an implant allows the enucleated orbit to better maintain the intraorbital pressure by counteracting the contracting processes[21] which begins almost immediately following the removal of the globe. The overall contraction of the orbital cavity after such an operation is easy to understand when one takes into consideration that the growth rate of the eye and of

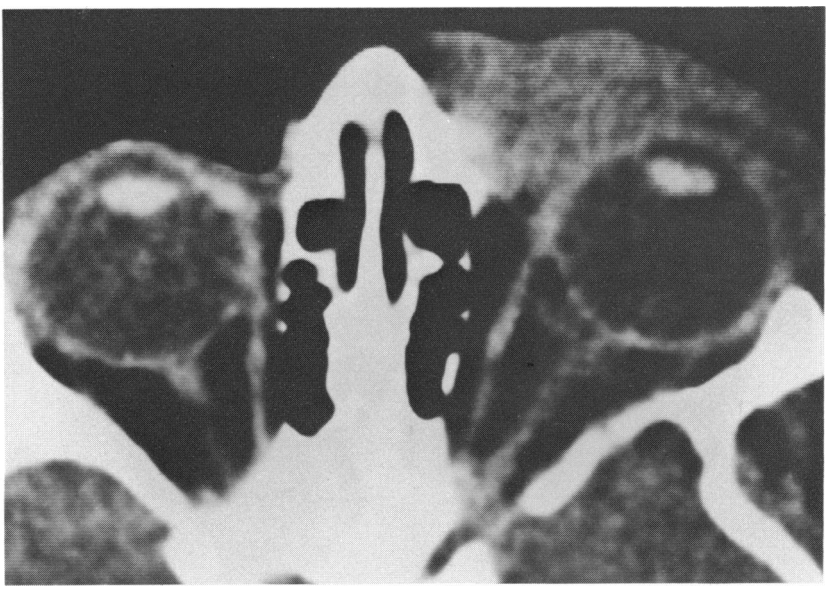


FIGURE 24
A 5-month-old girl with lymphangioma of left orbit. Volume of normal right orbit, 15.6 ml and volume of involved left orbit, 17.3 ml.

the bony orbit differ considerably. At birth, the human eyeball almost completely fills the small orbital cavity, sometimes even protruding from it (normal fetal exophthalmos). After birth, the eye quickly increases in volume about three times, reaching 70% of its adult size by as early as 4 years of age, whereas orbital growth continues at a much slower rate, until maturity has been reached.

Based on experimental findings,[4,13,21,25] the presence of the eye greatly influences the growth and normal development of the orbit. Consequently, enucleation performed in infancy and early childhood results in marked changes in orbital development. An implant placed at the time of enucleation leads to a more normally developed orbit and a better cosmetic appearance.[21,23,25,85] Pfeiffer[21] states that the overall orbital contraction after enucleation follows the law of adaptation (after a reduction of the orbital contents, the former orbital capacity need not be maintained any longer).

Additional studies by Kennedy[25,28,31] have verified Pfeiffer's observations. However, doubts have been raised as to whether or not orbital size is influenced by the absence of the globe. Spaeth,[86] in 1964, declared that

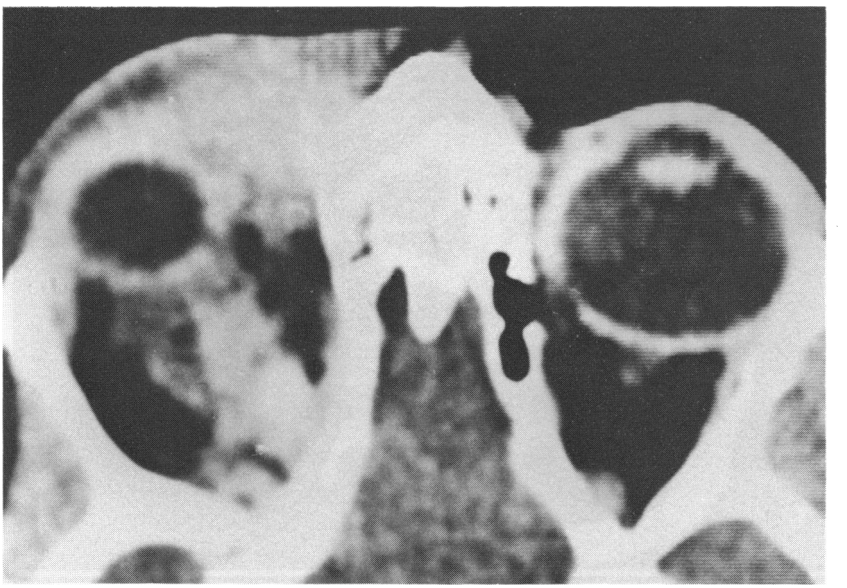


FIGURE 25
A 6-month-old boy with lymphangioma of right orbit. Volume of normal left orbit, 15.7 ml and volume of involved right orbit, 19.3 ml.

"it is absurd to state that the small bony orbits of congenital microphthalmos or anophthalmos is dependent upon the eyeball defect." Furthermore, he doubted that there is a direct relationship between the growth of the orbit and the presence of the eyeball. Sarnat and Shandeling[26] reported findings contrary to those presented by Pfeiffer.[21] The latter had reported that removal of the eye leads to an arrest in development and reduction in capacity of the involved orbit. Sarnat and Shandeling[26] observed that although the orbital size was smaller than the unoperated side, the involved orbit became progressively larger in growing animals with a longer postoperative survival period.

The ability to accurately determine orbital volume in the living state will allow us to study these problems more completely and answer these questions more definitively.

Orbital volume determinations are at the crux of the problem of treating anophthalmic patients. Kennedy[31] has aptly summarized the problem—"The oculoplastic surgeon attempts to correct the cosmetic blemish of the patient with an anophthalmic orbit by some type of surgical procedure. All of these procedures are aimed at increasing the orbital volume."

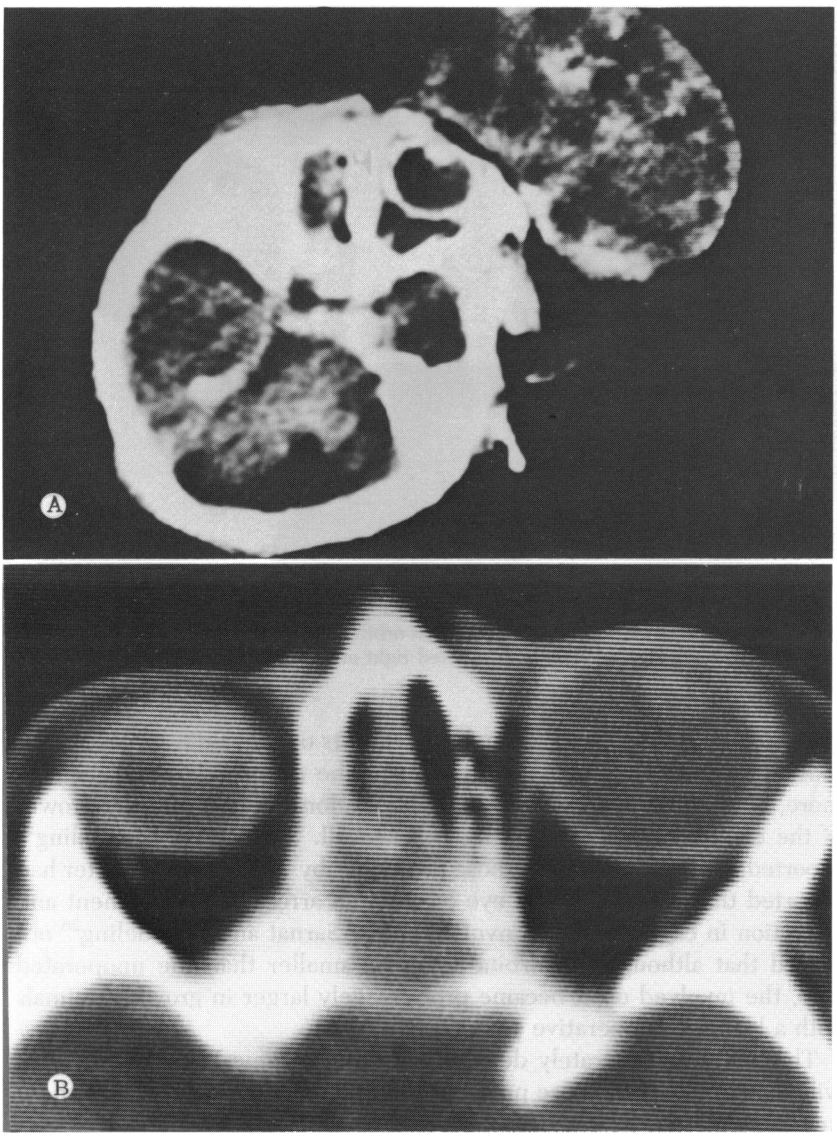


FIGURE 26

A: A 3-month-old girl with teratoma of left side of face. Possible orbital involvement was also suspected initially. Volume of normal right orbit, 16.1 ml and left orbit, 12.4 ml. B: After removal of facial lesion, ipsilateral right orbit was found to be normal in size and contralateral left orbit was noted to be smaller than normal because of microphthalmos on that side. Volume of normal right globe, 5.2 ml and volume of small left globe, 3.8 ml.

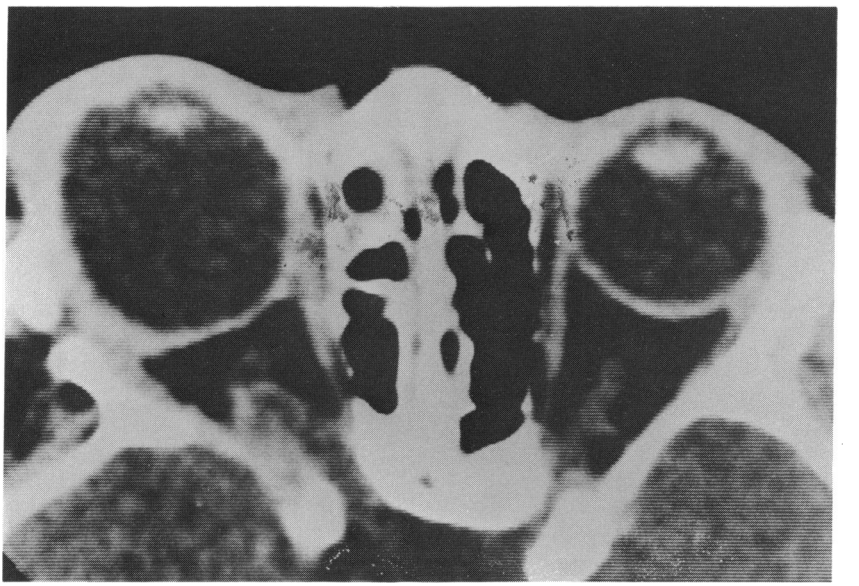


FIGURE 27
A 3-month-old boy with neurofibromatosis and secondary glaucoma in right eye. This resulted in buphthalmos on involved side and, in turn, enlarged globe caused a compensatory increase in orbital volume on that side. Volume of normal left orbit, 15.9 ml; and volume of involved right orbit, 18.5 ml; volume of normal left globe, 5.1 ml; and volume of enlarged right globe, 6.2 ml.

4. Study and treatment of the traumatized orbit.

Orbital fractures are one of the most common injuries observed in the facial region. The orbital volume may be increased or decreased as a result of this type of injury. Orbital capacity may be increased after a "blowout" fracture of the orbital floor.[87] This term is used to describe the "out" fracture of the orbital process of the maxilla that may occur after blunt injury to the orbit.[88] On occasion, "blow-in" fractures are observed in cases of orbital floor fractures. The mechanism of the blow-in fracture is the reverse of the blowout fracture, ie, bone fragments of the orbital floor are pushed into the orbital cavity as a result of increased pressure in the maxillary antrum secondary to trauma to the anterior maxilla. The resulting exophthalmos is produced by the decreased orbital cavity (reduced volume) which is no longer sufficient in capacity to house the globe and the orbital contents.

Radiation to the developing orbit is another form of trauma which gives rise to a striking decrease in orbital volume.[89,90] Radiation therapy follow-

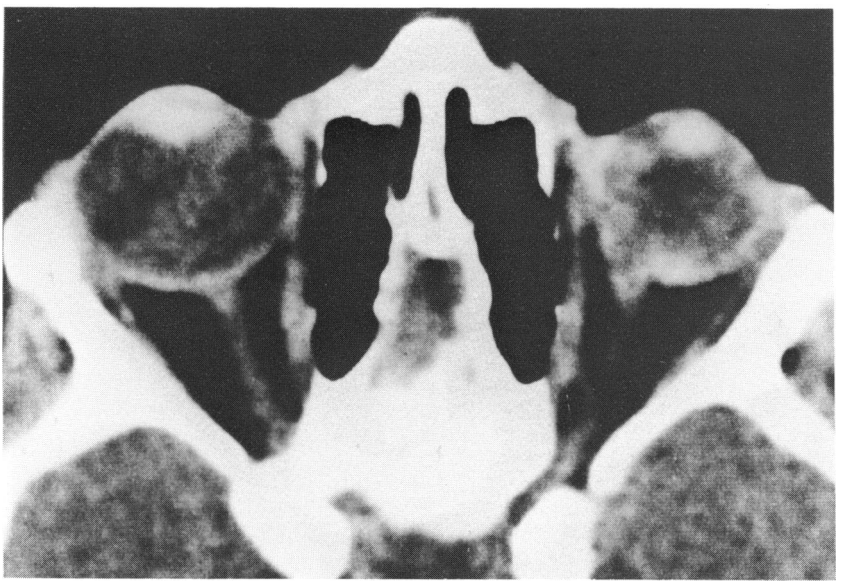


FIGURE 28
A 6-month-old boy with left microphthalmos and associated decrease in orbital size on this side. Volume of normal right orbit, 16.4 ml and and volume of involved left orbit, 14.7 ml.

ing enucleation in early childhood produces the worst possible conditions for the subsequent growth of the orbit. An analytical study of patients with retinoblastoma, treated with radiation following enucleation without implant, revealed a far greater orbital underdevelopment than is the case with simple enucleation.[89] The decrease of the orbital capacity and the slowing of skeletal growth as well as soft tissue atrophy as a result of radiation, cause facial asymmetry to a far greater extent than enucleation alone.[90]

5. Study and treatment of orbital soft tissue disorders.

This current study presents an accurate and reproducible method of determining bony orbital volume in the living state. However, this technique is equally applicable to soft tissue study of the orbital contents as well, and is the subject of the parallel study now in progress. This will have broad application in the management of those patients with Graves' disease who are candidates for orbital decompression. The volume increase in the extraocular muscles, orbital fat, lacrimal gland, etc, can be determined and the corresponding amount of decompression can be

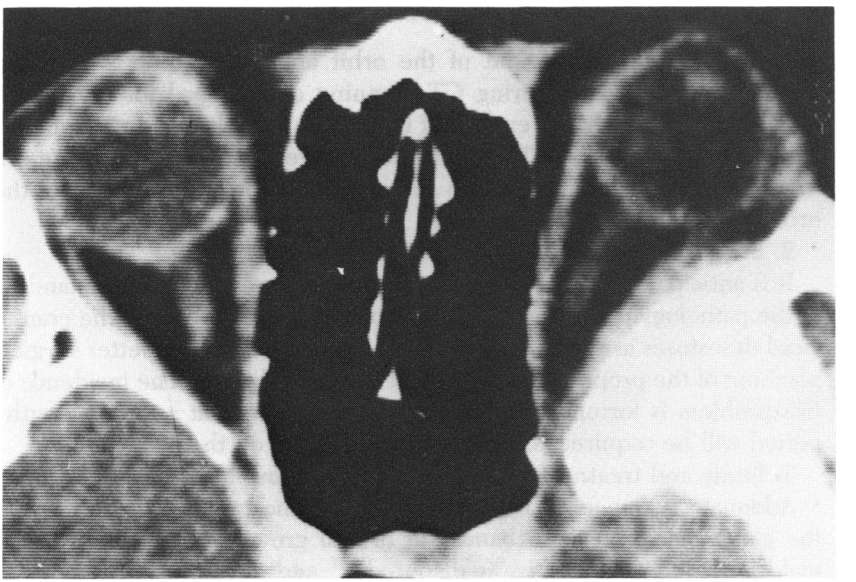


FIGURE 29
A 58-year-old woman with a left sphenoidal wing meningioma. Thickened bone encroaches into involved orbit significantly decreasing bony orbital volume. Volume of normal right orbit, 22.2 ml and and volume of involved left orbit, 19.4 ml.

tailored to the individual patients' needs. In addition, this technique will allow us to monitor the volumetric response of the orbital contents to nonsurgical treatments (systemic steroids, radiation, immunosuppressants, thyrotropic drugs, etc). Finally, the progression and/or regression of orbital tumor masses can be carefully defined and followed by this technique.

CLINICAL APPLICATIONS

While the primary intent of this thesis was to report a technique for *in vivo* determination of orbital volume, certain clinical situations have been encountered which lend themselves to assessment by this technique.

Earlier in this text, the various applications of this technique for the measurement, *in vivo*, of orbital bony and soft tissue volume have been presented. These clinical applications have been broken down into long-term and short-term studies in progress.

LONG-TERM STUDIES IN PROGRESS

1. Growth and development of the orbit and its contents. A limited number of children requiring CT scanning of the head for neurologic conditions are also being evaluated for orbital growth and development. This will require serial CT scans up to the age of 13 years and from it a more accurate assessment of the actual growth and development of the orbit and its contents will be made.

2. Study of congenitally malformed orbits.

It is anticipated that from this study will derive a better understanding of the pathology of premature closure of the cranial sutures—the craniofacial dysostoses as applied to the orbits. This will allow for better surgical planning of the proposed correction of these conditions. The incidence of this problem is fortunately low so it is anticipated that a rather lengthy period will be required to secure adequate data on these patients.

3. Study and treatment of the anophthalmic orbit.

Adequate evidence has been presented to indicate that early removal of the globe results in disturbances in orbital growth. The degree of the maldevelopment, however, is disputed[3-37] and current studies will, in time, accurately elucidate this problem. The role of the implant after enucleation is also being studied.

4. Study and treatment of the traumatized orbit is another long-range ongoing investigation.

Included in this study are those orbits whose growth has been altered (traumatized) by radiation therapy. Radiation to the developing orbit after enucleation gives rise to a striking decrease in orbital volume.[89,90] This technique will allow for an accurate determination of the amount of decrease and hopefully, correlating this with the amount of radiotherapy, will allow for better planning or fragmentation of the dosage to minimize orbital changes.

5. This technique is applicable to the determination of the volume of orbital soft tissues as well as bony volumetric measurements.

This is being carefully studied in a number of patients with Graves' disease. Changes in orbital soft tissues as a result of medical and surgical treatments will allow us to better understand the pathophysiology of this perplexing problem.

SHORT-TERM STUDIES IN PROGRESS

A number of clinical conditions result in orbital changes which require more immediate attention. While we are involved in long-term studies of the *in vivo* growth and development of the orbit, certain evaluations have

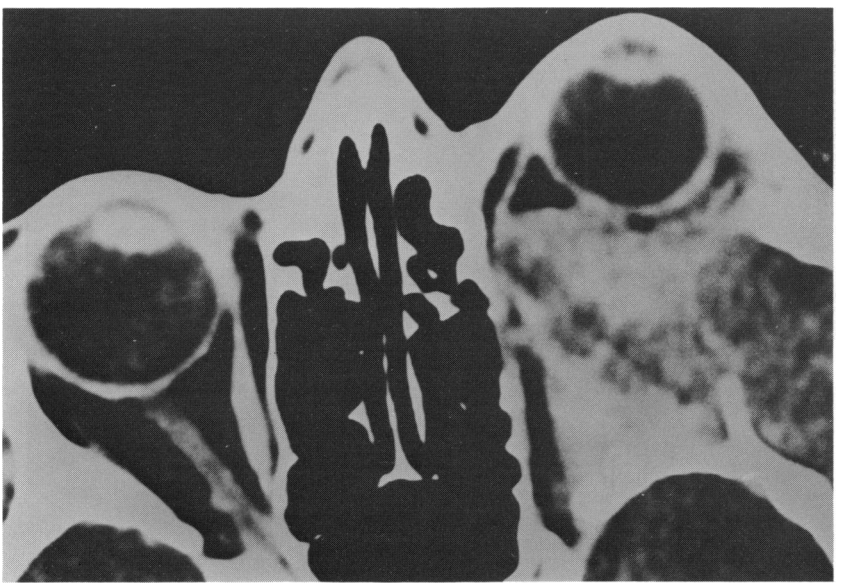


FIGURE 30
A 72-year-old woman with same diagnosis and similar findings as Fig 29. Volume of normal right orbit, 22.2 ml and and volume of involved left orbit, 12.7 ml.

been made on the basis of information currently available. The assessment of orbital volume changes by this technique have afforded us the opportunity to follow or treat these problems.

After puberty, when the cranial and facial bones have reached their adult status, only long-standing disease processes are capable of altering bony orbital volume (Figs 10 through 12).

Furthermore, if the responsible disease process is slow enough, the gradual enlargement of the orbit is capable of housing the increasing orbital soft tissues and the amount of secondary, compensatory exophthalmos is often negligible. This is well documented in Figs 13 to 17. Consequently, the amount of clinically observable exophthalmos is not always an accurate indication of the underlying pathology.

The therapeutic application of this technique is further illustrated by the following. A 36-year-old woman developed a biopsy-proven capillary hemangioma near the roof of the left orbit in infancy. The lesion subsequently regressed, but not before the orbit on that side had significantly enlarged. Subsequently, the left globe became lower than the right and 3 ml of enophthalmos was noted, as well as a deep left upper lid sulcus (Fig

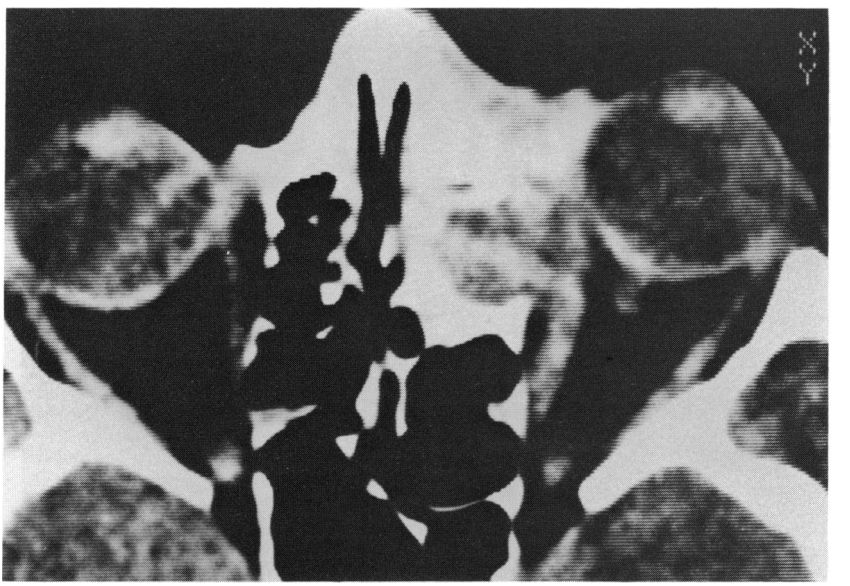


FIGURE 31
A 47-year-old woman with a mucocele of left ethmoid sinus which encroach into left orbit thereby reducing orbital volume on this side. Volume of normal right orbit, 22.1 ml and and volume of involved left orbit, 20.8 ml.

18). Orbital volume determinations revealed that the left orbit was 2.9 ml larger than the right (Fig 19). This volume disparity was corrected by the subperiosteal (orbital floor) insertion of an equal amount of silicone. The postoperative appearance is seen in Fig 20. In the future, the repair of the left upper lid ptosis will be undertaken.

On the other hand, rapidly growing orbital tumors in the adult do not permit enough time for compensatory bony orbital volume adaptive changes. In these instances, the amount of exophthalmos is a good clinical index of the amount and rate of growth of the mass lesion. This is clearly seen in an 88-year-old woman with a brief history of exophthalmos. Biopsy proved this to be a malignant melanoma of the orbit. The bony orbital volume is virtually identical so that the rapidly growing tumor mass was not present long enough to cause any measurable orbital volume changes (Fig 21).

Prior to age 13, alterations in the amounts of orbital tissue present causes rapid and profound changes in the bony orbital volume. Infants, in the first few months of life, have been found to have startling increases in orbital size from disease processes present for very short periods (Figs 22

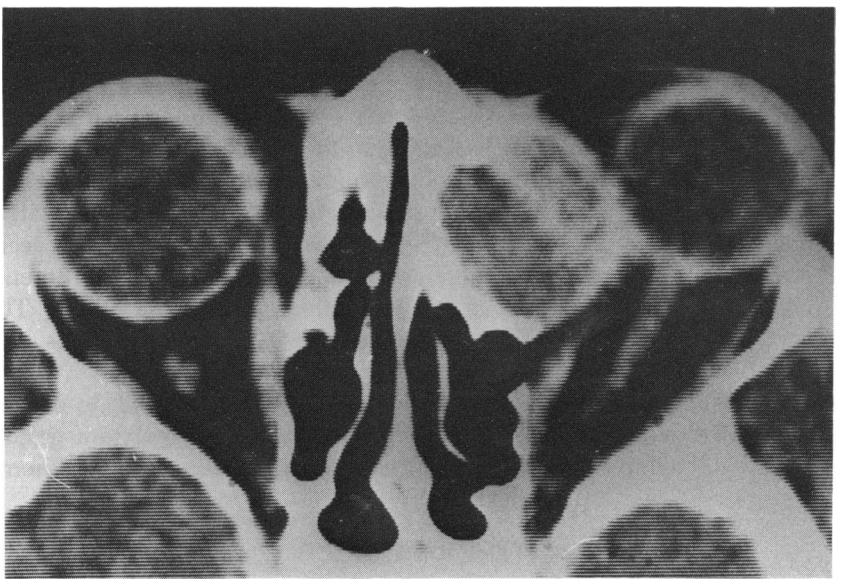


FIGURE 32
A 20-year-old woman with same diagnosis and findings as Fig 29. Volume of normal right orbit about 21.7 ml and and volume of involved left orbit about 19.4 ml; volume of mucocele, 4.0 ml.

to 25). Here, too, the amount of exophthalmos clinically present may not be a reliable indicator of the degree of the underlying process because the enlarged orbit reduces the exophthalmos which would otherwise be manifested.

The size of the globe is another important element in the growth and development of the orbit.[3-37] This fact has been elaborated upon extensively in an earlier portion of this thesis and is part of an ongoing clinical study of the normal and abnormal growth and development in this area (Figs 26 to 28).

Decreases in bony orbital volume are manifested clinically in the form of pseudoexophthalmos. In these conditions the orbital soft tissues and globe are normal but the bony box housing them has become smaller forcing them outward. Patients presenting this clinical problem are frequently thought to have real exophthalmos until subsequent investigation reveals otherwise. A number of clinical conditions involving the orbital bones may result in a decrease in bony orbital volume (Figs 29 to 32).

SUMMARY

The various congenital and acquired conditions which alter orbital volume are reviewed. Previous investigative work to determine orbital capacity is summarized. Since these studies were confined to postmortem evaluations, the need for a technique to measure orbital volume in the living state is presented. A method for volume determination of the orbit and its contents by high-resolution axial tomography and quantitative digital image analysis is reported. This procedure has proven to be accurate (the discrepancy between direct and computed measurements ranged from 0.2% to 4%) and reproducible (greater than 98%). The application of this method to representative clinical problems is presented and discussed.

The establishment of a diagnostic system versatile enough to expand the usefulness of computerized axial tomography and polytomography should add a new dimension to ophthalmic investigation and treatment.

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REFERENCES

1. Merkel F: *Handbuch der Topographischen Anatomie*. Braunschweig, 1891, vol 1, pp 74-76.
2. Popow: in Lesshaft P: *Grandlager der Theoretischen Anatomia*. Leipzig, W. Hartmann, 1842, p 99.
3. Byers W: Report of the Committee of the Ophthalmic Society on Excision. *Trans Ophthalmol Soc UK* 1898; 18:256-257.
4. Thomson WE: The determination of the influence of the eyeball on the growth of the orbit by experimental enucleation of one eye in young animals. *Trans Ophthalmol Soc UK* 1901; 21:258-263.
5. Wessely K: Beitrage zu den Wachstumsbe zu Hengen Zwischen dem Augapfel und Seinen Nachbarorganen. *Arch F Ophthalmol* 1922; 108:491-495.
6. Sattler CH: Operationen zur Verbesserund der Kosmetic Nach Enucleation. *Arch F Ophthalmol* 1922; 108:229-234.
7. Heckel EB: Enucleation in infants. Proceedings of the Pittsburgh Ophthalmological Society. *Am J Ophthalmol* 1922; 5:227.
8. Stieven K: Enucleation in infants. Proceedings of the Pittsburgh Ophthalmological Society. *Am J Ophthalmol* 1922; 5:227.
9. Koch C, Brunetti L: Étude des Correlations Morphologiques Entre L'Orbite et le Globe Oculaire. *Arch Ophthalmol* 1934; 51:809-815.
10. Vorisek ES: Maldevelopment of an orbit. *Am J Ophthalmol* 1933; 16:434.
11. Hartmann H: Ueber Versuche: Am Wachsenden Auge. *Klin Monatsbl Augenheilkd* 1918; 60:467-469.

12. Luza E: Det Einfluss der Enukleation auf die Entroickelung des Sehnervenkanals. *Klin Monatsbl Augenheilkd* 1938; 101:413-417.
13. Taylor WOG: The effect of enucleation of one eye in childhood upon the subsequent development of the face. *Trans Ophthalmol Soc UK* 1939; 59:361.
14. Gayat T: Eassais de Mensuration de L'Orbite. *Ann d'Ocul* 1873; 70:1-10.
15. Broca P: Recherches syrl'indice Orbitaire. *Arch Ophthalmol* (Paris) 1875, pp 368-370.
16. Weiss J: quoted in Whitnall SE: *The Anatomy of the Human Orbit,* ed 2. London, Oxford University Press, 1932.
17. Adachi B: Die Orbita und die Hauptmasse des Schadels der Japaner. *Z F Morphol Anthropol* 1904; 7:379-386.
18. P'an TH: Measurement of Chinese orbits. *J Anat* 1932-33; 17:596-600.
19. Whitnall SE: *The Anatomy of the Human Orbit,* ed 2. London, Oxford University Press, 1932.
20. Schultz AH: The size of the orbit and of the eye in primates. *Am J Phys Anthropol* 1940; 26:389-397.
21. Pfeiffer RL: The effect of enucleation on the orbit. *Trans Am Acad Ophthalmol Otolaryngol* 1945; 49:236-239.
22. Alexander JCC, Anderson JE, Hill JC, et al: The determination of orbital volume. *Trans Can Ophthalmol Soc* 1961; 24:105-113.
23. Sarnat BG, Shandeling PD: Postnatal growth of the orbit and upper face in rabbits (after exenteration of the orbit). *Arch Ophthalmol* 1965; 73:829-837.
24. Howard GM, Kinder RSL, Macmillan AS: Orbital growth after unilateral enucleation in childhood. *Arch Ophthalmol* 1965; 73:80-83.
25. Kennedy RE: The effect of early enucleation on the orbit in animals and humans. *Trans Am Ophthalmol Soc* 1964; 62:459. Also in *Am J Ophthalmol* 1965; 60:277-306.
26. Sarnat BG, Shandeling PD: Orbital volume following evisceration, enucleation and exenteration in rabbits. *Am J Ophthalmol* 1970; 70:787-799.
27. Sarnat BG: The imprint method to determine orbital volume in the rabbit. *Ophthalmologica* 1970; 160:142.
28. Kennedy RE: Growth retardation and volume determinations of the anophthalmic orbit. *Trans Am Ophthalmol Soc* 1972; 70:278-297.
29. Apt L, Isenberg S: Changes in orbital dimensions following enucleation. *Arch Ophthalmol* 1973; 90:393.
30. Osborne D, Hadden OB, Deeming LW: Orbital growth after childhood enucleation. *Am J Ophthalmol* 1974; 77:756-759.
31. Kennedy RE: Bone changes in the adult anophthalmic orbit influencing oculoplastic reconstructive considerations. *Trans Am Ophthalmol Soc* 1976; 74:237-250.
32. Wolff E: *The Anatomy of the Eye and Orbit*. Revised by R.J. Last 6th ed., Philadelphia, WB Saunders Co, 1900.
33. Hellman M: Changes in the human face brought about by development. *Int J Orthod Oral Surg* 1927; 13:475-482.
34. Ford EHR: Growth of the cranial base. *Am J Orthod* 1958; 44:498-505.
35. Morin JD, Hill JC, Anderson JE, et al: A study of growth in the interorbital region. *Am J Ophthalmol* 1963; 56:895-901.
36. Schaeffer JP: The clinical anatomy and development of the paranasal sinuses. *Penn Med J* 1936; 39:395-403.
37. vonLimborgh J, Tonneyck-Muller J: Orbital growth pattern in experimental microphthalmia. *Mod Probl Ophthalmol* 1975; 14:1-13.
38. Mann I: *Development of the Human Eye,* ed 2. London, Oxford University Press, 1949.
39. Barber A: *Embryology of the Human Eye*. St Louis, CV Mosby Co, 1955.
40. Mann I: *Developmental Abnormalities of the Eye,* ed 2. Philadelphia, JB Lippincott, 1957.
41. Blodi FC: Developmental anomalies of the skull affecting the eye. *Arch Ophthalmol* 1957; 57:593-610.
42. Pico G, Townsend W: Congenital and developmental anomalies of the orbit, in T Duane (ed): *Clinical Ophthalmology,* 1979, vol 2, chap 30, pp 1-11.

43. Duke-Elder S: Congenital deformities, in *System of Ophthalmology*. London, Kimpton, 1967, vol III, part 2, pp 415-445.
44. Blodi FC: Pathology of orbital bones. *Am J Ophthalmol* 1976; 81:1-18.
45. Archer DB, Gordon DS, Maguire CJF, et al: Ophthalmic aspects of craniostenosis. *Trans Ophthalmol Soc UK* 1974; 94:172-180.
46. Wolfe SA: A rationale for the surgical treatment of exophthalmos and exorbitism. *J Maxilofac Surg* 1977; 5:249-258.
47. Tessier P: Recent improvements in the treatment of facial and craniofacial deformities of Crouzon's disease and Apert's syndrome, in P Tessier, R Callahan, JC Mustarde, K Salyer (eds): *Symposium on Plastic Surgery in the Orbital Region*. St Louis, CV Mosby Co, 1976, pp 271-290.
48. ———: Anatomical classification of facial, craniofacial and laterofacial clefts, in P Tessier, A Callahan, JC Mustarde, K Salyer (eds): *Symposium on Plastic Surgery in the Orbital Region*. St Louis, CV Mosby Co, 1976, pp 271-290.
49. Morse PH, Walsh FB, McCormick JR: Ocular findings in hereditgary diaphyseal dysplasia (Engelmann's Disease). *Am J Ophthalmol* 1969; 68:100-104.
50. Hartman DC: Anophthalmos and microphthalmos. *Proceedings of the Second International Symposium on Plastic and Reconstructive Surgery of the Eye and Adnexa*. St Louis, CV Mosby Co, 1967, pp 514-517.
51. Hare R: Congenital bilateral anophthalmos. *Arch Ophthalmol* 1943; 30:320-330.
52. Brunetti L: La Profondimetria Comparata Delle Due Orbite. *Ann Radiol Diag* 1931; 4:145-149.
53. Hartmann E, Gilles E: *Roentgenologic Diagnosis in Ophthalmology*. Philadelphia, JB Lippincott, 1959.
54. Tadmor R, New PFJ: Computed tomography of the orbit with special emphasis on coronal sections. Part 1. Normal anatomy. *J Comput Assist Tomogr* 1978; 2:24-36.
55. Walser RL, Ackerman LV: Determination of volume from computerized tomograms: Finding the volume of fluid-filled brain cavities. *J Comput Assist Tomogr* 1977; 1:117-125.
56. Heymsfield SB, Fulenwider T, Nordlinger B, et al: Accurate measurement of liver, kidney and spleen volume and mass by computerized axial tomography. *Ann Int Med* 1979; 90:185-194.
57. Olmsted JMH: *Calculus with Analytic Geometry*. Norwalk, CT, Appleton-Century-Crofts, 1966, vol 2, p 483.
58. Selby SM: *Standard Mathematical Tables*. Cleveland, The Chemical Rubber Company, 1968, p 19.
59. Keppel E: Approximateing complex surfaces by triangulation of contour lines. *IBM J Res Development* 1975; 19:2-15.
60. Fuchs H, Kedem ZM, Uselton SP: Optimal surface reconstruction from planar contours. *Comm ACM* 1977; 10:693-700.
61. Cook L, Cook PN, Lee RK, et al: Volume estimation: A new, accurate computerized algorithm. *Doctoral Thesis*, Departments of Diagnostic Radiology and Cardiology, The University of Kansas Medical Center, 1979.
62. Newman WM, Sproull RF: *Principles of Interactive Computer Graphics*. New York, McGraw-Hill, 1973.
63. Weibel ER, Eias E: *Quantitative Methods in Morphology*. New York, Springer-Verlag, 1967.
64. Walk L: Roentgenologic determination of the liver volume. *Acta Radiol* 1961; 35:49-57.
65. ———: Roentgenologic determination of liver volume: Simplified method of calculation. *Acta Radiol (Diagnosis)* 1967; 6:369-373.
66. ———: Assessment of liver size. *Digestion* 1968; 1:209-214.
67. Rollo FD, DeLand FH: The determination of liver mass from radionuclide images. *Radiology* 1968; 91:1141-1150.
68. Eilkman EA, Mack GA, Jain VK, et al: Computer assisted mass estimation from gamma-camera images. *J Nucl Med* 1979; 20:144-149.

69. Keats TE, Enge IP: Cardiac mensuration by the cardiac volume method. *Radiology* 1965; 85:850-856.
70. King DL, Al-Banna SJ, Larach DR: A new three-dimensional random scanner for ultrasonic/computer graphic imaging of the heart, in DN White, R Barnes (eds): *Ultrasound in Medicine*, Vol II. New York, Plenum Press, 1976.
71. King DL, Wai PM: Computer reconstruction of three-dimensional echocardiographic models of the left ventricle: Technical description and initial results using patient data. *Proceedings of the American Institute of Ultrasound in Medicine*. September 1980, p 53.
72. McLachlan MSF, Williams ED, Fortt AW, et al: Estimation of pituitary gland dimensions from radiographs of the sella turcica. *Br J Radiol* 1968; 41:323-349.
73. Dichiro G, Nelson KB: The volume of the sella turcica. *Am J Roentgenol* 1962; 87:989-995.
74. Fisher RL, DiChiro G: The small sella turcica. *Am J Roentgenol* 1969; 91:996-1000.
75. Austin JHM, Gooding CA: Roentgenographic measurement of skull size in children. *Radiology* 1971; 99:641-651.
76. Lusted LB, Keats TE: *Atlas of Roentgenographic Measurement*. Third edition, Chicago, Yearbook Medical Publishers, 1972, p 143.
77. Reese DF, O'Brien PC, Beeler GW Jr, et al: An investigation for extracting more information from computerized tomography scans. *Am J Roentgenol Radium Ther Nucl Med* 1975; 124:177-188.
78. Walser RL: Automatic interpretation of reconstructed objects: Finding the volume of brain ventricles. *Master Thesis*, Department of Information Engineering, University of Illinois at Chicago. *Circle*, 1975.
79. DeVoe AG: Experiences with surgery of the anophthalmic orbit. *Am J Ophthalmol* 1945; 28:1346-1351.
80. Soll DB: Asbell RL: Enophthalmos, in P Tessier, A Callahan, JC Mustarde, K Salyer (eds): *Symposium on Plastic Surgery in the Orbital Region*. St Louis, CV Mosby Co, 1976, pp 141-145.
81. Culler AM: Basic principles of anatomy and physiology of the orbit and relation to implant surgery. *Trans Am Acad Ophthalmol Otolaryngol* 1952; 56:17-20.
82. DeVoe AG: Repair of orbital deformities with glass wool. *Arch Ophthalmol* 1947; 38:245-247.
83. Smith B, Obear M, Leone CR: The correction of enophthalmos associated with anophthalmos by glass bead implantation. *Am J Ophthalmol* 1967; 64:1088-1093.
84. Wood-Smith D: Reconstruction of the orbital skeleton in anophthalmos, in P Tessier, A Callahan, JC Mustarde, K Salyer (eds): *Symposium on Plastic Surgery in the Orbital Region*. St Louis, CV Mosby Co, 1976, pp 177-179.
85. Tessier P: The definitive plastic surgical treatment of the severe facial deformities of craniofacial dysostoses. *Plast Reconstr Surg* 1971; 48:419-438.
86. Spaeth EB: Surgical pathology of the eyelids and the orbit in early childhood. *J Pediatr Ophthalmol* 1964; 1:9-16.
87. Pfeiffer RL: Roentgenography of exophthalmos, with notes on roentgenray in ophthalmology. *Trans Am Ophthalmol Soc* 1941; 39:492-497.
88. Smith B, Converse JM: Early treatment of orbital floor fractures. *Trans Am Acad Ophthalmol Otolaryngol* 1957; 61:602-608.
89. Ameniya T, Matsumura M, Hirose Y: Effects of radiation after enucleation without implantation on orbital development of patients with retinoblastoma. *Ophthalmologica* (Basal) 1977; 174:137-145.
90. Ellsworth RM: Orbital growth. *Proceedings of the Second International Symposium on Plastic and Reconstructive Surgery of the Eye and Adnexa*. St Louis, CV Mosby, 1967, p 511-513.