A New and Validated CT-Based Method for the Calculation of Orbital Soft Tissue Volumes

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PURPOSE. There is no consensus as how to calculate orbital soft tissue volume based on CT or MRI scans. The authors sought to validate their technique and to assess the intraobserver and interobserver variability of their calculations of bony orbital volume (OV), orbital fat volume (FV), and extraocular muscle volume (MV) on CT scans of humans.

METHODS. The authors calculated these volumes with the use of a manual segmentation technique on CT scans with commercially available software. Two observers (one of them masked) calculated the orbital soft tissue volumes in a CT scan of a phantom constructed of dry skull, butter, and chicken muscle. These calculations were compared with previously taken standard volume measurements of these materials. Repetitive calculations on one CT scan by the same observer were compared. Soft tissue volumes taken from 10 orbital CT scans were calculated by two observers and compared. From the data acquired, intraobserver and interobserver variability was calculated.

RESULTS. Outcomes of these calculations using this software approximated the volumes of the phantom measured with standardized techniques. Accuracy of the phantom calculations between the two observers varied from +0.7% to −0.7% for FV and between −1.5% and −2.2% for MV. Mean differences between the repeated calculations were smaller than 5%. The intraclass correlation coefficient varied from 0.961 to 0.999.

CONCLUSIONS. Calculating orbital soft tissue volume using a manual segmentation technique for CT scans is a reliable and accurate tool. (*Invest Ophthalmol Vis Sci.* 2008;49: 1758–1762) DOI:10.1167/iovs.07-1030

The volume of orbital soft tissue can change in common orbital diseases such as Graves orbitopathy (GO) and orbital myositis or as a consequence of enucleation of the eyeball.[1] Calculation of orbital soft tissues volumes in, for instance, patients with GO may be helpful in understanding the etiology and pathogenesis of the disease.

Most investigators calculate orbital volume using software that is either custom built or provided by the CT scanner manufacturer. In the literature,[2] different methods such as manual outlining (a technique usually referred to as manual segmentation), computer-assisted segmentation, and computer-assisted border detection are used. However, these techniques have been poorly validated. Ramieri et al.[3] used commercially available software (Mimics; Materialise, Louvain, Belgium) to calculate orbital bony volume (OV) and fat volume (FV) in patients with enophthalmia after blow out fractures. Their calculations were comparable to those of other authors, but they did not validate their method.

Mimics (Materialise) software is an image-processing package with three-dimensional (3D) image visualization function that interfaces with all common scanner formats; it is a general purpose segmentation program for gray value images and can process any number of 2D image slices. The software enables the user to control and correct the segmentation of CT data and MRI data. No technical knowledge is needed for creating 3D images on a display screen resulting from computerized reconstructions of medical objects.[4] The focus of the Materialise company is to build software for industrial purposes, but for their medical division they developed software for the manufacturing of physical models by means of stereolithography prosthesis manufacturing, dental implant planning and placement, orthopedic and major facial reconstructions after cancer surgery, and reconstructive surgery in case of congenital deformity. Until now, Mimics (Materialise) had not been used for the calculation of extraocular muscle volume (MV).

The purpose of this study was to investigate the usefulness of the Mimics (Materialise) software for the calculation of orbital soft tissue volume by validation of this method and to determine the intraobserver and interobserver variability of the calculations.

PATIENTS, MATERIALS, AND METHODS

Materials

To validate the computerized calculations provided by the Mimics (Materialise) software, we constructed a phantom of butter and chicken wing muscles as equivalents for, respectively, orbital fat and extraocular muscles. Butter was cut in solid state, in a block of $20 \times 20 \times 30$ mm, representing a volume of 12,000 mm³. Four chicken wings were prepared to provide small muscle bundles surrounded by an adventitial sheath. The muscle volume was determined by volume displacement in a calibrated oil bath and measured 2900 mm³. Before scanning, the muscles were inserted in the butter at room temperature using a glass rod. Care was taken not to insert air bubbles. After packing in thin plastic foil, the butter/muscle complex was inserted in the orbital cavity of a human skull. With the skull placed in the position customarily used for a patient's head, spiral CT scans were made. The fat (butter) volume and the muscle volume were calculated as described in this article.

Patients

Spiral CT scans of 10 orbits of eight patients with a variety of orbital diseases (e.g., Graves orbitopathy, phthisis bulbi, orbital trauma, choroidal melanoma, optical nerve glioma) were selected randomly from our outpatient clinic; normal orbits were used except for the four orbits of the patients with Graves orbitopathy. The Medical Ethical Commission considered this not subject to consent, and the research adhered to the tenets of the Declaration of Helsinki. CT scans had been obtained in the course of routine clinical care using a multislice spiral CT scanner (Mx8000 IDT; Philips, Eindhoven, The Netherlands). Continuous scanning with a slice thickness of 1.3 mm and a slice increment of 0.7 mm had been applied. Patients were in the supine position, with the scan plane parallel to the plane containing the lines interconnecting the outer external meatus and the lateral eye corner on each side of the head. No gantry tilt was applied. Patients were asked to look at a fixed point. Axial images were burned on a CD-ROM and were loaded into a workstation (XW 4300; Hewlett-Packard, Wilmington, DE) situated in the ophthalmological department and independent of the CT scanner. Mimics (Materialise) version 9.11 was used to calculate the orbital soft tissue volume.[4]

Measurement Methods

A soft tissue window (grayscale) setting was used to discriminate among orbital muscle, fat, and bone tissue. Orbital soft tissue CT numbers were set at -200 to $+100$ Hounsfield units (HU) for bony orbital volume, -200 to -30 HU for fat tissue, and -30 to $+100$ HU for muscle tissue. The optimum threshold was the CT number halfway between the CT numbers of the tissues to be separated. As a result, the tissues of interest were highlighted on the display in specific colors using so-called masks. A mask contained tissue with the chosen CT number in all the slices of the three image stacks and changed color each time a major process, such as region growing or subtraction, was completed. Region growing (computer-assisted separation of different tissues) and manually deleting tissues were used until only the tissue of interest remained. The volume of the 3D reconstruction was expressed in cubic millimeters to two decimals. Three-dimensional visual control of the measurements could be performed at any moment during the measurements. This allowed the observer to visually check the result of the calculations. Instead of outlining the structures of interest in every slice, as most investigators (summarized in Bijlsma et al.[2]) have done, the structures that were not relevant were deleted using a variety of tools. The program showed axial, coronal, and sagittal images on the same display screen (Figs. 1, 2l–n). Segmentation performed in one image stack automatically appeared in the other two. To get a good result, the observer had to work with all three image stacks. The software calculated the tissue volume by means of voxel addition and reconstructed a 3D image that was displayed on the computer screen.

Volume Calculation Method

The volume calculation method is as follows: For axial images, start at the mid-orbit and work upward and downward. For coronal images, work anteriorly and posteriorly from the mid-orbit. For sagittal images, work from medial to lateral.

Bony orbital volume is measured as follows:

1. Use a mask setting of -200 to $+100$ HU. All the soft tissues inside and outside the bony orbit (fat, muscle neural tissue, eyeball) are visible. Save this mask for use in other tissue measurements (Fig. 2a).
2. Duplicate the mask (Fig. 2b).
3. Determine the bony borders of the orbit, and separate them from the remaining skull in the image stack. Perform coarse manual outlining with a lasso (Fig. 2b). Apply the multislice tool, remove tissue in 20 or 30 or more slices at once, and save (Fig. 2c). Subtract this mask from the original saved mask (before duplicating). Within seconds, the area of interest is shown (Fig. 2d).

4. Determine the orbital aditus with the following landmarks: frontal bone, frontozygomatic suture, inferior orbital rim, anterior lacrimal crest (Figs. 2e, 2f). Erase every pixel outside this border.
5. The orbital volume is limited by cutting off the optic nerve at the entrance of the optic canal and by cutting off the pterygopalatine fossa (Fig. 2i) and the superior and inferior orbital fissures (Figs. 2e, 2h, 2i).
6. Generate 3D reconstruction (conical shape) of the bony orbital content (Fig. 2h).

Fat volume is measured as follows:

1. Use a mask setting of -200 to -30 HU. Change the CT number in the very first mask.
2. Subtract from this mask the second saved mask (Fig. 2c) generated in OV, and save the result.
3. Erase the remaining extraorbital fat by deleting fat tissue in the skin of the eyelids and fat in the superior and inferior orbital fissures (Fig. 2j).
4. Generate 3D reconstruction of the orbital fat tissue.

Extraocular muscle volume is measured as follows:

1. If FV is subtracted from OV (Fig. 2d), the volume of muscles, neurovascular structures, and the eyeball will remain and are already outlined in all slices (Figs. 2k–n).
2. Erase the nonmuscular structures, except for the tendons and aponeuroses, which are to be cut away as soon as they touch the sclera. The oblique muscles are excluded because they are difficult to separate from the eyeball and make no significant contribution to the muscle volume.[5] The levator palpebrae is cut away, together with the superior rectus.
3. Generate the 3D reconstruction of the rectus muscle.

Phantom Calculations

For the calculations of the FV and MV of the phantom, measurements were obtained by an unmasked observer (NR) and a masked observer (PK). PK was masked for the volume used in the phantom. The accuracy of the volume calculations using manual segmentation and the Mimics (Materialise) software was assessed by comparing the known volumes of the phantom with those calculated by the two observers.

Intraobserver and Interobserver Variability

For intraobserver variability, observer NR calculated the volume of one patient with a normal orbit on 10 consecutive working days. Intraobserver variability was expressed using the coefficient of variation, here calculated as the SD divided by $100\times$ the mean of the measurements, for the percentage $\times100\%$.

For interobserver variability, the calculations of two observers were analyzed. NR calculated the FV, MV, and OV, of 10 orbits twice with an interval of 2 to 10 days. Thereafter, the second observer PK performed the same calculations independently on the same orbits.

Statistical Analysis

A statistical computer program (SPSS 12.0.2 for Windows; SPSS Inc., Chicago, IL) was used for statistical analysis. Intraclass correlation coefficients and their 95% confidence intervals were calculated for all parameters to determine the intraobserver and interobserver variability (two-way mixed-effects model; 0 = no agreement, 1 = perfect agreement between measurement occasions or observers). Absolute magnitude of the measurement error between the observers was calculated with the method Bland and Altman.[6]
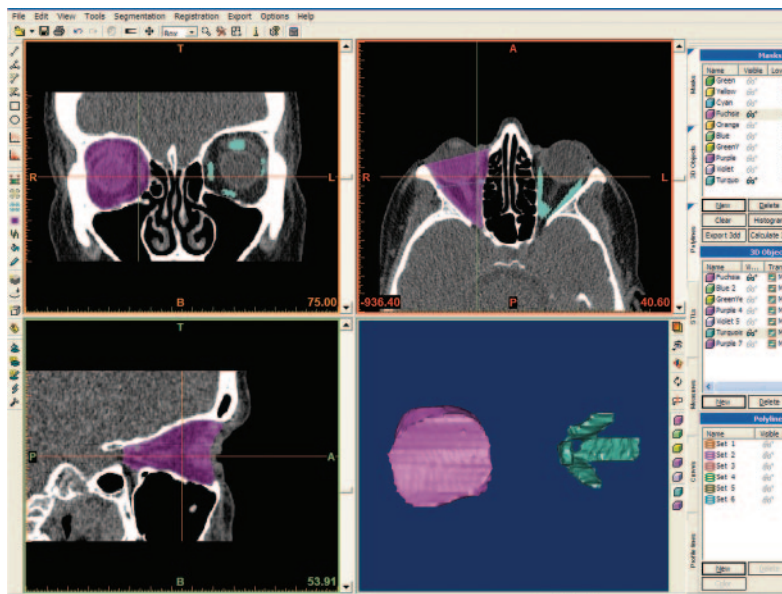
FIGURE 1. Overview of the display screen with the axial, coronal, and sagittal CT slices with the highlighted segmented tissues (*fuchsia pink*, OV; *turquoise,* MV), and the 3D reconstruction of the segmented tissues. *Left*: tool icons; *right*: color mask icons.

RESULTS

Phantom Calculations and the Measurement Method

The HU units of the butter (-94 HU mean) and the chicken muscles ($+20$ HU mean) were within the range of human orbital fat and extraocular muscles. The known volume of the fat was 12.0 mL; observer NR calculated 12.1 mL (difference, $+0.7\%$), and the blinded observer PK calculated 11.9 mL (difference, -0.7%). The known volume of muscle was 2.9 mL; NR calculated 2.85 (difference, -1.5%), and PK calculated 2.83 mm^3 (difference, -2.2%).

Intraobserver Variability

For the orbital fat, muscle, and bony volumes of one orbit, observer NR found the respective values of 18.58 ± 0.11 mL (range, $18.38 - 18.76$), 3.03 ± 0.05 mL (range, $2.97 - 3.10$), and 25.17 ± 0.06 mL (range, $25.10 - 25.24$). Mean differences expressed in percentages were 0.6% for FV, 1.65% for MV, and 0.24% for OV. Intraobserver variability of the two calculations on the 10 different orbits was 0.97% for FV (range, $0.2 - 2.0$), 2.6% for MV (range, $0.3 - 4.0$), and 0.98% for OV (range, $0.3 - 2.7$).

Interobserver Variability

Interobserver variability is shown in Table 1. Note the good agreement between the two observers, though in the Bland and Altman plots, observer PK calculated the OV volume consistently smaller than did observer NR ($0.1 - 0.6$ mL; Fig. 3). The results of observer PK ameliorated over time (Fig. 2).
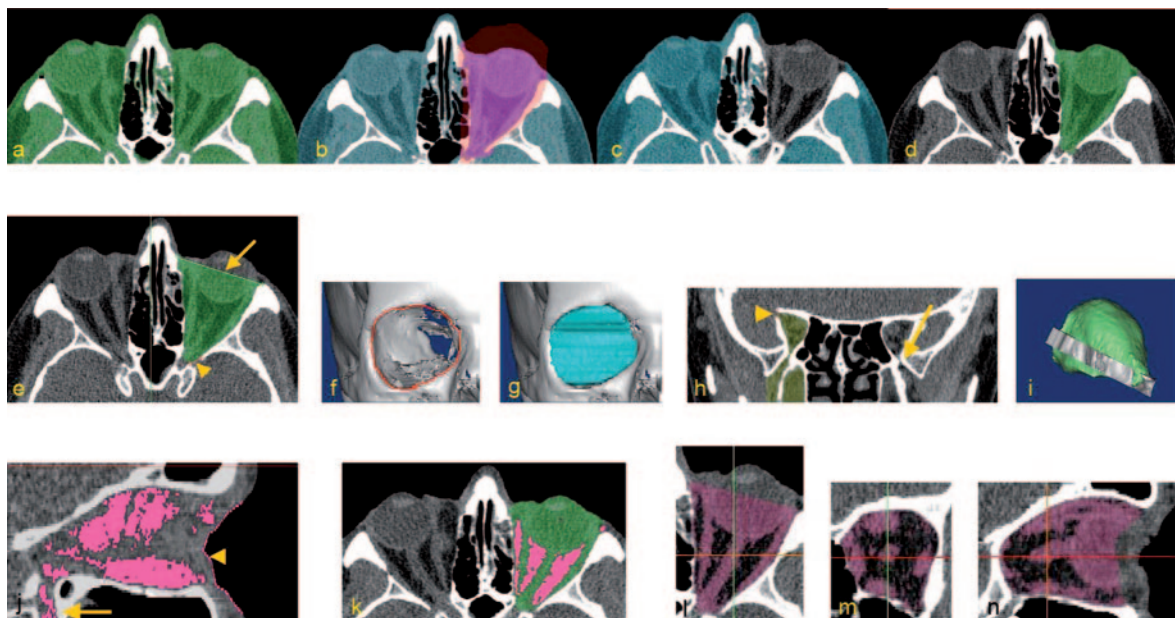

FIGURE 2. (**a**) Mask -200 to $+100$ HU. (**b**) Duplicate mask and multislice outline. (**c**) Remove. (**d**) Subtract [(**a**) $-$ (**c**)]. (**e**) Manual erase outside bony orbit. *Arrow*: line anterior lacrimal crest to fronto-zygomatic bone. *Arrowhead*: superior orbital fissure. (**f**, **g**) Orbital aditus. (**h**) Good visibility orbit to pterygo-palatine fossa (*arrow*) and superior orbital fissure (*arrowhead*). (**i**) 3D orbital bony volume with adjacent bone ring (*gray*). (**j**) Fatty material in skin (*thin line*; *arrowhead*), infraorbital fossa (*arrow*). Subtract [(**d**) $-$ (**j**) = (**k**)]. (**l**–**n**) Muscles to be cleaned.

TABLE 1. Intraclass Correlation Coefficient (ICC) of Measurements by NR (Observer 1 and 2) and by PK (Observer 3)

	ICC 1–2	ICC 1–3	ICC 2–3	ICC 1–2–3
FV	0.999	0.999	0.999	0.998
MV	0.994	0.961	0.955	0.970
OV	0.998	0.980	0.984	0.987

ICC outcome values: 0 = no agreement; 1 = perfect agreement.

DISCUSSION

Validation

We validated the commercially available software program Mimics (Materialise) as a technique for calculations of orbital soft tissue based on CT scans and found it accurate and precise. Intraobserver and interobserver variability were acceptable.

Compared with our validation, previous validations were less sophisticated. Other investigators used a variety of calibration materials, such as silicone blocks (Forbes et al.[7,8]) or glass strips (Krahe et al.[9]). Lutzemberger and Salvetti[10] used rabbit muscle for their validation, which best resembled the human in vivo situation thus far. We validated the software by constructing a phantom. Given that orbital fat is soft, we chose full cream butter that can be cut in blocks in the solid state after cooling and that is soft at room temperature. Muscles can be inserted in the soft material. The calculations of a masked observer differed minimally from the known volume (fat, 0.7%; muscle, −2.2%).

Mimics (Materialise) is a user-friendly program with a steep learning curve. By using a sequence of colored masks, the observer can always go back to the previous mask in case of a mistake or a computer problem. The 3D reconstructions enable the user to check at any moment the correctness of the segmentations, and there is no need for the user of this program to understand its technical details. Because Mimics (Materialise) can use CD-ROMs or DVDs for loading images, it can process any stack of images and is therefore independent of a scanner. The workstation and the program can be used outside the radiology department.

Because there is no consensus about how to measure orbital soft tissue in patient scans, there is no standard program for comparison. For instance, calculation of the OV requires a cutoff of the bony volume at the orbital aditus. This cutting process results in a larger volume if it is performed with sagittal images rather than axial images. Given that calculations in the literature[7-11] are based on axial images, we decided to use axial images as well. It is difficult to separate the tendon of a rectus muscle from the eyeball, so we did not include it and cut the muscle short the moment it touched the eyeball. The most difficult part for the calculation procedure is the superior complex. It is difficult to separate the rectus superior from the levator palpebrae muscle. We chose the trochlea as landmark. Above the trochlea, no superior rectus is present. This seems justified because the bulk of the levator lies behind the cutting point where the rectus superior and the levator touch the eyeball.

Intraobserver/Interobserver Variability

The calculations of fat by the two observers showed great similarity and could detect small changes in FV. OV also showed little difference, but, according to the Bland and Altman plot, the calculated volumes of PK were constantly smaller than the calculated volumes of NR, which meant that the landmarks of the bony orbit were different between the two observers. MV is difficult to calculate. For the measurements of MV and OV, some knowledge of anatomy is necessary. The differences between the two observers were largely attributed to a lack of knowledge of the anatomy of the orbit. In addition, the results of the second observer ameliorated during the course of the experiment, so the measurements were within the target of 5% difference. It is imperative that borders be set and measurements be carried out according to a strict protocol. Intraobserver variability was also tested in repetitive calculations. This was possible because measurements of a stack of images can be deleted completely without any trace.

CONCLUSIONS

Mimics (Materialise) is a valuable tool for the calculations of orbital soft tissue volume. Because it can be used on any stack of images, comparisons of CT scans and MRI scans are possible. Intraobserver variability was less than 5% for the calculations of FV, MV, and OV. Interobserver variability did improve with better knowledge of anatomy and strict adherence to the segmentation protocol.
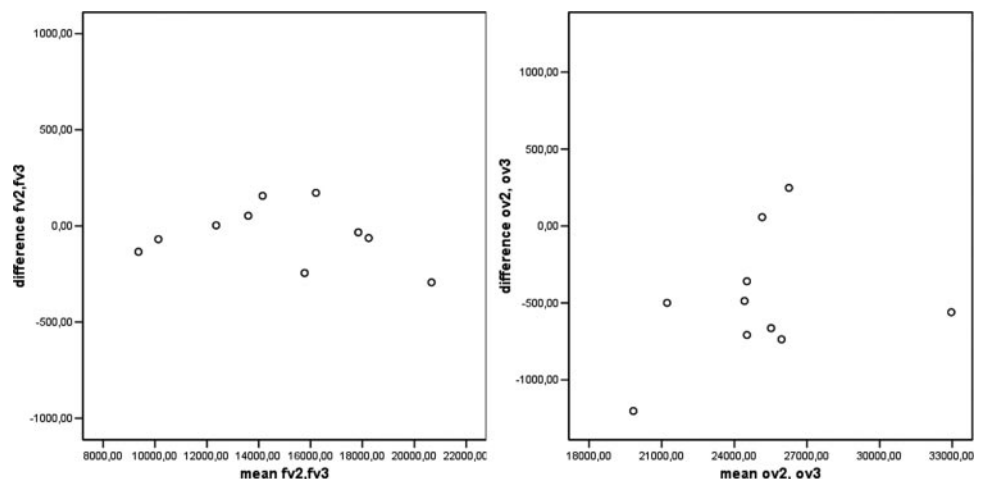

FIGURE 3. Bland and Altman plot of FV and OV. The FV plot shows all points around zero. In the OV plot, most points are below zero.

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E R R A T U M

Erratum in: "*Nrl*-Knockout Mice Deficient in Rpe65 Fail to Synthesize 11-*cis* Retinal and Cone Outer Segments" by Feathers et al. (*Invest Ophthalmol Vis Sci.* 2008;49:1126–1135.)

In Figure 7C, the positions of the data should be switched. The traces in the $Rpe65^{-/-}/Nrl^{-/-}$ column should be in the $Rpe65^{-/-}$ column, and the traces in the $Rpe65^{-/-}$ column should be in the $Rpe65^{-/-}/Nrl^{-/-}$ column. The corrected figure is printed below.