Age and gender-specific reference values of orbital fat and muscle volumes in Caucasians

Regensburg, N.I.; Wiersinga, W.M.; van Velthoven, M.E.J.; Berendschot, T.T.J.M.; Zonneveld, F.W.; Baldeschi, L.; Saeed, P.; Mourits, M.P.

DOI
10.1136/bjo.2009.161372

Publication date
2011

Document Version
Final published version

Published in
British journal of ophthalmology

Age and gender-specific reference values of orbital fat and muscle volumes in Caucasians

Noortje I Regensburg,[1] Wilmar M Wiersinga,[2] Mirjam E J van Velthoven,[1] Tos T J M Berendschot,[3] Frans W Zonneveld,[4] Lelio Baldeschi,[1] Peerooz Saeed,[1] Maarten P Mourits[1]

[1]Orbital Centre, Department of Ophthalmology, Academic Medical Centre, University of Amsterdam, The Netherlands
[2]Department of Endocrinology and Metabolism, Academic Medical Centre, University of Amsterdam, The Netherlands
[3]University Eye Clinic Maastricht, Maastricht, The Netherlands
[4]Department of Radiology, University Medical Centre, University of Utrecht, The Netherlands

Correspondence to
Dr Noortje Regensburg, Orbital Centre, Department of Ophthalmology, Academic Medical Centre, University of Amsterdam, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands; n.i.regensburg@amc.nl

Accepted 19 October 2009
Published Online First
2 December 2009

ABSTRACT

Aim To provide age and gender-specific reference values for orbital fat and muscle volumes (MV) in Caucasian adults.

Patients and Methods Computed tomographic scans of 160 orbits from 52 men and 55 women, aged 20–80 years, not affected by orbital disease were evaluated. Orbital bony cavity volume (OV), fat volume (FV) and MV were calculated by a previously validated method using the software program Mimics. Ratios of FV to OV and of MV to OV were determined.

Results OV, FV and MV were all significantly larger in men than in women ($p<0.001$), but FV/OV and MV/OV were similar in both sexes. OV and MV did not change with age, but FV increased with advancing age in both women ($p<0.001$) and men ($p<0.001$). Linear regression analysis with FV/OV and MV/OV ratios as dependent variables and age and gender as independent variables showed a significant correlation between age and FV/OV ($r=0.52$, $p<0.0001$) and age and MV/OV ($r=-0.26$, $p=0.001$).

Conclusions Advancing age is associated with an increase of FV/OV and a minor decrease of MV/OV. Gender-specific differences in orbital FV and MV disappear once FV and MV are related to OV, by calculating the ratios FV/OV and MV/OV. Age-specific gender-neutral reference ranges (2.5 and 97.5 percentiles) of FV/OV and MV/OV are presented.

Volumetry of orbital soft tissues can be helpful in the evaluation of the natural course or the response to treatment of particular orbital diseases. Volumetry can also be very useful for a better understanding of disease pathogenesis. A good example is Graves' orbitopathy (GO).[1] Volumetry has been proposed as an independent outcome measure in trials assessing the efficacy of immunosuppressive treatment or radiotherapy in GO.[2] Volumetry in GO can also be applied to assess the relative contributions of fat and muscle to the overall increase of orbital tissues. There are few studies in this respect,[3–6] but the available data suggest that not all GO patients have enlarged eye muscles; there may exist a subset of patients with just fat enlargement.[6 7]

It is obvious that reference ranges of orbital fat and muscle volumes (MV) in healthy subjects are required in order to distinguish between enlarged and not enlarged orbital fat and MV in patients. Reference ranges of orbital volumes have been reposted in several studies.[8–13] A number of limitations, however, prevent generalisation of these reference ranges. First, there are important racial differences. Asians have shallower orbits than Caucasians and consequently Von Lanz *et al*[14] found higher mean orbital bony cavity volumes (OV) in Caucasian than in Japanese adults (27 cm^3 and 23 cm^3, respectively). Second, there may be gender and age-specific differences in orbital volumes. Although volumes of men and women are often reported separately, age is usually not taken into account and race is not always mentioned. Therefore, the aim of the present study is to provide age and gender-specific reference values of orbital volumes in adult Caucasians.

PATIENTS AND METHODS

The CT scans of all patients visiting the Academic Medical Center of the University of Amsterdam, between 2002 and 2007, who underwent orbital CT scanning in the course of routine clinical care according to a fixed protocol, were reviewed. The local medical ethical committee considered this study not a subject of consent. The research adhered to the tenets of the Declaration of Helsinki.

CT scans of adults older than 20 years, who had at least one orbit without pathology, were Caucasians and had intact orbital walls, were included. CT scans were excluded in the case of non-Caucasian origin, systemic or malignant disease, recent trauma, silent sinus syndrome, any neoplasm involving the bony orbit or the orbital tissues, recent orbital wall fracture and previous paranasal sinus or squint surgery or gantry tilt in CT scanning. Common indications for CT scanning in the final study population concerned post-enucleation socket syndrome, nasal polyps, longstanding orbital blowout fractures, skull trauma or nasal fractures. Subjects were stratified into six age groups 20–29 years, 30–39 years, 40–49 years, 50–59 years, 60–69 years and 70+ years.

CT images were burned on a CD-ROM and loaded into a HP XW 4300 workstation. Fat volume (FV), MV and OV were calculated according to a validated protocol, using Mimics 11.1 software.[15 16] The applied software is an image-processing package with three dimensional (3D) image visualisation functions that interfaces with all common scanner formats and can be used for the segmentation of grey value images. All calculations were performed by one observer. The intra and interobserver variability for this method was low, provided the observer adheres strictly to the protocol.[15] The intraclass correlation coefficient of this variability was FV=0.99 and 0.99, MV=0.99 and 0.96 and OV=0.99 and 0.98, respectively.

Table 1 Orbital FV, orbital MV, OV and their ratios in 160 normal Caucasian orbits

	Male orbits (n=72)		Female orbits (n=88)		
	Mean	SD	Mean	SD	p Value
FV (cm^3)	16.2	3.4	14.0	2.9	<0.001
MV (cm^3)	4.2	0.5	3.7	0.5	<0.001
OV (cm^3)	28.9	2.4	24.9	2.2	<0.001
FV/OV	0.56	0.11	0.56	0.10	ns
MV/OV	0.15	0.02	0.15	0.02	ns

p Values represent the significance of the Student's t test.
FV, fat volume; MV, muscle; OV, orbital bony cavity volume.

Statistical analysis

Absolute and relative frequencies were used to describe categorical data. Numerical data were summarised by their means and standard deviations. Differences between means were tested using analysis of variance and Student's t test. The relation between orbital volumes (OV, FV, MV), the ratios FV/OV and MV/OV, age and gender were further evaluated using linear regression analysis.

RESULTS

The CT scans of 160 orbits from the whole cohort (n=500 scans) met the inclusion criteria. The orbits were derived from 52 men and 55 women; there was no significant mean age difference between the orbits of the different genderd (mean age±SD in male orbits was 47.2±15.6 and in female orbits 49.2±16.7, p=0.43). Of the 88 female orbits, 42 were right sided and 46 left; for the male orbits, 37 were right and 35 left sided. Mean FV, MV and OV were all larger in men than in women, but no difference was observed in the ratios FV/OV and MV/OV (table 1).

In both genders, advancing age was associated with increasing FV, whereas MV and OV were not related to age (table 2 and figure 1). The ratio FV/OV increased with advancing age in both genders, whereas the ratio MV/OV decreased slightly with advancing age in women but not in men (table 2).

Linear regression analysis was performed with the ratios MV/OV and FV/OV as dependent variables, and both age and gender as independent variables. Age showed a significant correlation for FV/OV (r=0.52, p<0.0001). For FV/OV this correlation was independent of gender. MV/OV showed a statistically significant, negative correlation in women, but none in men (table 2). Figure 2 shows MV/OV and FV/OV as a function of age, together with the regression lines and the 2.5 and 97.5 percentile (P) boundaries. The formulae for the boundaries are: FV/OV=0.227+0.0034*age for P2.5 and FV/OV=0.5695+0.0034*age for P97.5. MV/OV=0.1281−0.00027*age for P2.5 and MV/OV=0.1922−0.00027*age for P97.5.

Reference ranges of the ratios FV/OV and MV/OV for the ages of 20–80 years are listed in table 3 as percentiles 2.5 and 97.5.

DISCUSSION

This study provides reference values of orbital soft tissue volumes in Caucasians in relation to gender and age. The average Caucasian OV in men (28.9±2.5 cm^3) was larger than in women (24.9±2.2 cm^3). These values compare reasonably well with those provided by von Lanz *et al*[14] (range 28.9–31 cm^3 for men and women together) and are clearly higher than found by Furuta[17] (23.6±2.0 cm^3 and 20.9±1.3 cm^3) in Japanese men and women.

The effect of age on OV has been studied in the Japanese and Chinese populations.[17,18] The authors found a strong direct linear correlation between age and OV (p<0.05), which continued after the age of 40 years. The OV was calculated from horizontal, transverse and anterior–posterior distances at different levels in the scans. In our study, however, with computer-assisted region growing and segmentation, we found no correlation between OV and age (men r=0.053, p=0.66; women r=0.15, p=0.18).

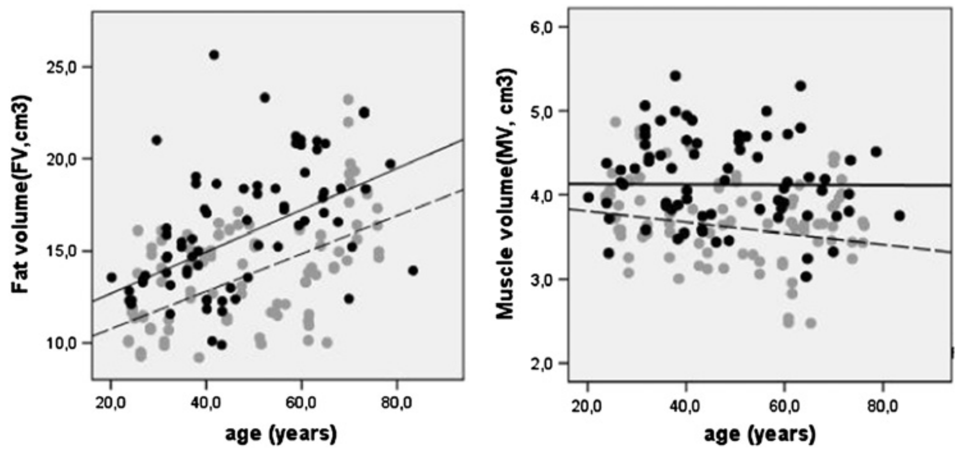
Distinct gender differences in FV and MV of 'Europeans' (presumably Caucasians) have previously been reported by Krahe *et al*.[19] The authors found a mean orbital FV of 11.2 cm^3 in men and 10.1 cm^3 in women. Their volume of the four rectus muscles was 2.2 cm^3 in men and 1.5 cm^3 in women. In

Table 2 Orbital volumes and volume ratios for different age strata per gender

			Orbital volumes (in cm^3, mean and P(2.5)–(97.5))						Ratios (mean and P(2.5)–(97.5))			
	Age, years	n	OV	P(2.5)–(97.5)	FV	P(2.5)–(97.5)	MV	P(2.5)–(97.5)	FV/OV	P(2.5)–(97.5)	MV/OV	P(2.5)–(97.5)
Men	20–29	9	28.4	25.5–31.3	13.8	8.33–19.4	4.01	3.33–4.69	0.49	0.31–0165	0.14	0.11–0.17
	30–39	18	29.4	24.7–34.2	15.2	11.5–18.8	4.34	3.18–5.49	0.52	0.41–0.63	0.15	0.11–0.19
	40–49	15	27.5	23.4–31.6	14.4	6.0–22.7	4.11	3.07–5.14	0.52	0.27–0.77	0.15	0.11–0.19
	50–59	13	29.9	24.4–35.3	18.7	13.7–23.7	4.31	3.44–5.17	0.63	0.45–0.81	0.15	0.11–0.18
	60–69	11	29.5	23.1–35.9	18.0	13.1–23.0	4.07	2.66–5.46	0.61	0.47–0.76	0.14	0.11–0.17
	70+	6	27.9	24.3–31.7	18.7	11.5–25.9	4.04	3.34–4.72	0.67	0.45–0.88	0.14	0.12–0.17
R			0.053		0.50		−0.12		0.55		−0.17	
p Value			ns		<0.001		ns		<0.001		ns	
Women	20–29	15	24.4	21.8–27.0	11.9	7.6–16.1	3.86	3.0–4.7	0.49	0.34–0.63	0.16	0.13–0.19
	30–39	16	24.9	20.7–29.1	13.1	8.5–17.7	3.78	2.8–4.8	0.52	0.39–0.65	0.15	0.13–0.17
	40–49	14	24.7	20.6–28.8	14.5	10.5–18.5	3.72	2.7–4.7	0.59	0.44–0.74	0.15	0.12–0.18
	50–59	11	24.2	22.0–26.5	12.9	8.2–17.7	3.56	2.7–4.4	0.53	0.36–0.71	0.15	0.11–0.18
	60–69	21	25.5	19.5–31.5	14.6	7.6–21.5	3.52	2.4–4.6	0.57	0.36–0.78	0.14	0.11–0.17
	70+	11	25.3	19.9–30.6	17.2	13.7–20.7	3.77	3.1–4.5	0.68	0.56–0.80	0.15	0.12–0.18
R			0.15		0.50		−0.21		0.53		−0.35	
p Value			ns		<0.001		ns		<0.001		0.001	

R is the Pearson correlation coefficient between age and the orbital volumes and volume ratios.
p Values show the significance of the correlation.
FV, fat volume; MV, muscle volume; OV, orbital bony cavity volume; P, percentile.

Figure 1 Scatter plots depicting correlation between age and fat volume (FV) and muscle volume (MV) per gender (black spots, male; grey spots, female; continuous line, male FV y=0.112*×+10.932, MV y=−0.004*×+4.37; interrupted line, female. FV y=0.087*×+9.687; MV y=−0.006*×+3.993).



our study FV was also larger in men (16.1 cm^3) than in women (14.0 cm^3) and MV was larger in men (4.2 cm^3) than in women (3.7 cm^3).

We observed a significant increase of FV with advancing age, whereas MV was slightly dependent on age only in women. Tian *et al*[12] divided 21 subjects into three age groups, namely 19–35, 39–55 and 59–70 years. They calculated normal orbital soft tissue volumes from MRI scans, and observed that orbital fatty tissue did not differ significantly in these three age groups. However, there were only seven subjects per age group. Hamedani,[20] on the other hand, stated in his review article that there is a natural involution of orbital fat with age. We were not able to confirm this in our series, because we found that the FV increased with age. This may be due to a different method of calculation, because we noticed that the orbital fat in the older age group bulged into the eyelids due to the laxity of the orbital septum. This fat is, however, still orbital fat because it lies within the boundaries of the orbital septum. Darcy *et al*,[13] in a recent publication, reported that the inferior periocular soft tissue area anterior to the anteroposterior globe axis increased with age. The largest contribution to this size increase was fat expansion. Their observations provide supporting evidence that orbital fat expansion occurs with age.

The difficulty in comparing normal orbits with pathological orbits is the fact that 'normal' orbital volumes are highly variable (OV range 20.7–34.5 cm^3; FV range 9.2–25.7 cm^3; MV range 2.47–5.42 cm^3), because they are age and gender dependent. Therefore, we calculated the ratios FV/OV and MV/OV. These ratios show the relative amount of volume that FV and MV occupy in the orbit and effectively abolish the gender differences. Regression analysis showed that these ratios are still dependent on age. Consequently, we constructed age-dependent reference values for the FV/OV and MV/OV ratios. Applying percentiles 2.5 and 97.5 will allow judgement as to whether or not the FV and MV of an individual patient should be considered abnormal.

A possible bias in our series may have been that in the majority of cases the contralateral orbit was not 'normal', but to recruit 160 healthy people for a CT scan is not considered ethical. We scrutinised the subject files before selection for disorders that were known to influence the orbit and/or orbital contents, and excluded these subjects from the present analysis.

CONCLUSION

In both women and men there are changes in normal orbital soft tissue volumes with increasing age. FV increases in both men and women, whereas MV remains stable in men but decreases in women. Although men have larger orbits, more FV and more MV than women, the ratios for FV/OV and MV/OV show the same trend with age in both genders. Therefore, these ratios may be of value in studying orbital disease.

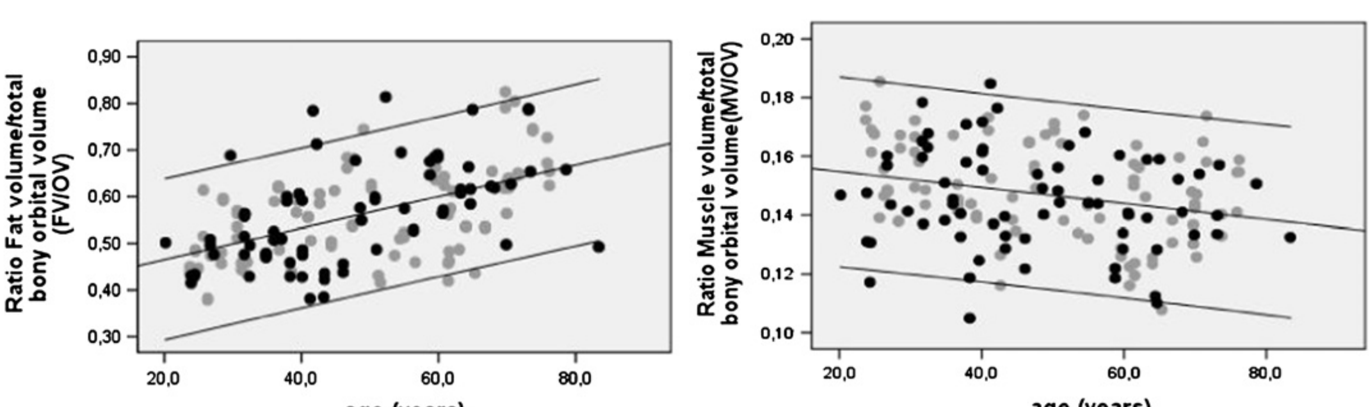


Figure 2 Scatter plots depicting correlation between age and the ratios fat volume/orbital cavity volume (FV/OV) and muscle volume/orbital cavity volume (MV/OV) per gender (black spots, male; grey spots, female). The middle lines are regression lines (FV/OV y=0.00337*×+0.3902; MV/OV y=−0.00027*×+0.1602). The upper and lower lines show the 97.5 and 2.5 percentile boundaries.

Table 3 Reference ranges of orbital FV and MV ratios (FV/OV, MV/OV) for ages 20–80 years in percentiles (2.5 and 97.5)

Age, years	FV/OV (P2.5)	FV/OV (P97.5)	MV/OV (P2.5)	MV/OV (P97.5)
20	0.30	0.64	0.12	0.19
21	0.30	0.64	0.12	0.19
22	0.30	0.64	0.12	0.19
23	0.31	0.65	0.12	0.19
24	0.31	0.65	0.12	0.19
25	0.31	0.65	0.12	0.19
26	0.32	0.66	0.12	0.19
27	0.32	0.66	0.12	0.18
28	0.32	0.66	0.12	0.18
29	0.33	0.67	0.12	0.18
30	0.33	0.67	0.12	0.18
31	0.33	0.67	0.12	0.18
32	0.34	0.68	0.12	0.18
33	0.34	0.68	0.12	0.18
34	0.34	0.69	0.12	0.18
35	0.35	0.69	0.12	0.18
36	0.35	0.69	0.12	0.18
37	0.35	0.70	0.12	0.18
38	0.36	0.70	0.12	0.18
39	0.36	0.70	0.12	0.18
40	0.36	0.71	0.12	0.18
41	0.37	0.71	0.12	0.18
42	0.37	0.71	0.12	0.18
43	0.37	0.72	0.12	0.18
44	0.38	0.72	0.12	0.18
45	0.38	0.72	0.12	0.18
46	0.38	0.73	0.12	0.18
47	0.39	0.73	0.12	0.18
48	0.39	0.73	0.12	0.18
49	0.39	0.74	0.11	0.18
50	0.40	0.74	0.11	0.18
51	0.40	0.74	0.11	0.18
52	0.40	0.75	0.11	0.18
53	0.41	0.75	0.11	0.18
54	0.41	0.75	0.11	0.18
55	0.41	0.76	0.11	0.18
56	0.42	0.76	0.11	0.18
57	0.42	0.76	0.11	0.18
58	0.42	0.77	0.11	0.18
59	0.43	0.77	0.11	0.18
60	0.43	0.77	0.11	0.18
61	0.43	0.78	0.11	0.18
62	0.44	0.78	0.11	0.18
63	0.44	0.78	0.11	0.18
64	0.44	0.79	0.11	0.17
65	0.45	0.79	0.11	0.17
66	0.45	0.79	0.11	0.17
67	0.45	0.80	0.11	0.17
68	0.46	0.80	0.11	0.17
69	0.46	0.80	0.11	0.17
70	0.47	0.81	0.11	0.17
71	0.47	0.81	0.11	0.17
72	0.47	0.81	0.11	0.17
73	0.48	0.82	0.11	0.17
74	0.48	0.82	0.11	0.17
75	0.48	0.82	0.11	0.17
76	0.49	0.83	0.11	0.17
77	0.49	0.83	0.11	0.17
78	0.49	0.83	0.11	0.17
79	0.50	0.84	0.11	0.17
80	0.50	0.84	0.11	0.17

FV, fat volume; MV, muscle volume; OV, orbital bony cavity volume; P, percentile.

Competing interests None.

Ethics approval This study was conducted with the approval of the Amsterdam Medical Centre Ethics Committee.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1. **Nugent RA,** Belkin RI, Neigel JM, *et al*. Graves orbitopathy: correlation of CT and clinical findings. *Radiology* 1990;**177**:675–82.
2. **Gorman CA.** Temporal relationship between onset of Graves' ophthalmopathy and diagnosis of thyrotoxicosis. *Mayo Clin Proc* 1983;**58**:515–19.
3. **Forbes G,** Gorman CA, Brennan MD, *et al*. Ophthalmopathy of Graves' disease: computerized volume measurements of the orbital fat and muscle. *AJNR Am J Neuroradiol* 1986;**7**:651–6.
4. **Breiman RS,** Beck JW, Korobkin M, *et al*. Volume determinations using computed tomography. *AJR Am J Roentgenol* 1982;**138**:329–33.
5. **Feldon SE,** Weiner JM. Clinical significance of extraocular muscle volumes in Graves' ophthalmopathy: a quantitative computed tomography study. *Arch Ophthalmol* 1982;**100**:1266–9.
6. **Zonneveld FW,** Koornneef L, Wittebol-Post D. Quantitative volumetric assessment of orbital soft tissue. *Proceedings CAR* 1991:181–7.
7. **Peyster RG,** Ginsberg F, Silber JH, *et al*. Exophthalmos caused by excessive fat: CT volumetric analysis and differential diagnosis. *AJR Am J Roentgenol* 1986;**146**:459–64.
8. **Bite U,** Jackson IT, Forbes GS, *et al*. Orbital volume measurements in enophthalmos using three-dimensional CT imaging. *Plast Reconstr Surg* 1985;**75**:502–8.
9. **Forbes G,** Gehring DG, Gorman CA, *et al*. Volume measurements of normal orbital structures by computed tomographic analysis. *AJR Am J Roentgenol* 1985;**145**:149–54.
10. **Kolk A,** Pautke C, Schott V, *et al*. Secondary post-traumatic enophthalmos: high-resolution magnetic resonance imaging compared with multislice computed tomography in postoperative orbital volume measurement. *J Oral Maxillofac Surg* 2007;**65**:1926–34.
11. **Ramieri G,** Spada MC, Bianchi SD, *et al*. Dimensions and volumes of the orbit and orbital fat in posttraumatic enophthalmos. *Dentomaxillofac Radiol* 2000;**29**:302–11.
12. **Tian S,** Nishida Y, Isberg B, *et al*. MRI measurements of normal extraocular muscles and other orbital structures. *Graefes Arch Clin Exp Ophthalmol* 2000;**238**:393–404.
13. **Darcy SJ,** Miller TA, Goldberg RA, *et al*. Magnetic resonance imaging characterization of orbital changes with age and associated contributions to lower eyelid prominence. *Plast Reconstr Surg* 2008;**122**:921–9.
14. **Von Lanz T,** Wachsmuth W. *Praktische anatomie*. 1st edn. Berlin: Springer-Verlag, 1979.
15. **Regensburg NI,** Kok PH, Zonneveld FW, *et al*. A new and validated CT-based method for the calculation of orbital soft tissue volumes. *Invest Ophthalmol Vis Sci* 2008;**49**:1758–62.
16. **Anon.** *Mimics. [Computer Program]. Version 10.2*. Leuven, Belgium: Materialise, 2007.
17. **Furuta M.** Measurement of orbital volume by computed tomography: especially on the growth of the orbit. *Jpn J Ophthalmol* 2001;**45**:600–6.
18. **Chen Z,** Zheng XH, Xie BJ, *et al*. [Study on the growth of orbital volume in individuals at different ages by computed tomography] (in Chinese). *Zhonghua Yan Ke Za Zhi* 2006;**42**:222–5.
19. **Krahe T,** Schlolaut KH, Poss T, *et al*. [Computed tomographic volumetry of the orbit in endocrine orbitopathy] (in German). *Rofo* 1989;**151**:597–601.
20. **Hamedani M,** Pournaras JA, Goldblum D. Diagnosis and management of enophthalmos. *Surv Ophthalmol* 2007;**52**:457–73.

Age and gender-specific reference values of orbital fat and muscle volumes in Caucasians

Noortje I Regensburg, Wilmar M Wiersinga, Mirjam E J van Velthoven, et al.

Br J Ophthalmol 2011 95: 1660-1663 originally published online December 2, 2009
doi: 10.1136/bjo.2009.161372