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Computer Analysis of Orbital Fat and Muscle Volumes in Graves Ophthalmopathy

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A technique using special computer programs and data from high-resolution computed tomographic scans has been developed that provides accurate and reproducible volume measurements for muscle and fat in the orbit. Normal values for retrobulbar fat and muscle were established in 19 adults. Nineteen patients with Graves exophthalmopathy were then studied, and a spectrum of change was found that included varying degrees of increased muscle volume or increased volume of both muscle and fat. Further categorization of these changes related to clinical characteristics should lead to a better understanding of the mechanism for ophthalmopathy in Graves disease.

The asymmetric pattern and distribution of orbital muscle enlargement that may occur in Graves disease has been effectively demonstrated by computed tomography (CT) [1]. The medial and inferior rectus muscle groups are more likely to be involved, though multiple views including reformatted or direct sagittal oblique images may be necessary to show the full extent of the changes [2]. CT has also been useful in excluding neoplasm and in differentiating endocrine changes from inflammatory disease or pseudotumor, although the latter situation may still be difficult [3].

The nature of the process that causes endocrine ophthalmopathy remains unclear. There is no clear relation between the level of thyroid function and progression or regression of ophthalmopathy as revealed by CT scanning. Histopathologic study of extraocular muscles in Graves patients shows varying amounts of edema, mononuclear cell infiltration, mucopolysaccharides, and fibrosis [4]. Electromyographic studies have revealed myopathic [5, 6] and true neuropathic [7] patterns. Changes in orbital fat, however, have received less attention. Trokel and Jakobiec [8] described a single case of increased retrobulbar fat, but they challenged existing views that a part of the exophthalmos is due to water drawn into the orbital fat by mucopolysaccharide deposition.

All previous assessments of muscle enlargement have been made subjectively or by single-plane dimension measurements. No attempts to measure orbital fat have been reported. CT has been used to make volume measurements of large viscera by summing cross-sectional areas and calculating pixel volumes [9]. More sophisticated programming may be introduced to define anatomic boundaries for three-dimensional volume calculations of smaller objects [10, 11]. Our goal has been to introduce refined programming in high-resolution orbital CT to calculate ocular muscle and fat volumes in normal patients and in those with various clinical manifestations of endocrine ophthalmopathy.

Subjects and Methods

Volume measurements were derived from CT scan data obtained with a GE 8800 system. Axial scans were made through the orbits and consisted of 30 adjacent 1.5 mm slices at 0° to −10° from the orbitomeatal base line. Contrast medium containing 42 g of iodine was administered intravenously. The digital data were transferred to our research computer system and image display devices for further analysis. Computer programs were developed using processing techniques known as region-growing, neighborhood-sampling, and automatic-tracing algorithms for boundary display. A range of CT attenuation numbers was specified in Hounsfield units for fat, muscle, and bone (fig. 1A). The muscle range included neural and vascular components of similar density. From a designated starting point within a structure, the program determined if neighboring adjacent pixels fell within the specified range. Each pixel within the range was included in the volume survey and generated additional neighbors for testing (fig. 1B). This process continued until the region grew to its boundaries or to a specific boundary set by the operator (fig. 1C). Pixels were summed from all slices and multiplied by a conversion factor (0.00096 cm^3/pixel for the 0.8 mm × 1.5 mm pixel) for volume measurement. This figure represented the total volume for fat or muscle in the orbit (fig. 1D).

A second technique was used to estimate the bony orbital volume (although region-growing could have been used). This approach utilized an automatic-tracing algorithm to trace the boundary between soft tissue and orbital wall [12]. The anterior boundary of the orbit on each slice was designated as the straight line connecting the lateral and medial orbital bones. As above, the calculated volume was the total of all pixels within the boundaries of all slices multiplied by the conversion factor.

To test the programs a phantom was constructed from a cone-shaped plastic cup. Pencils in the cup simulated muscles. Measured amounts of water within the cup simulated orbital fat and were easily differentiated from the pencils in the scans. Numerous scans and volume calculations wer obtained with different amounts of water to determine intrinsic method error and observer variability.

We used this technique to evaluate 38 adult patients (76 orbits),

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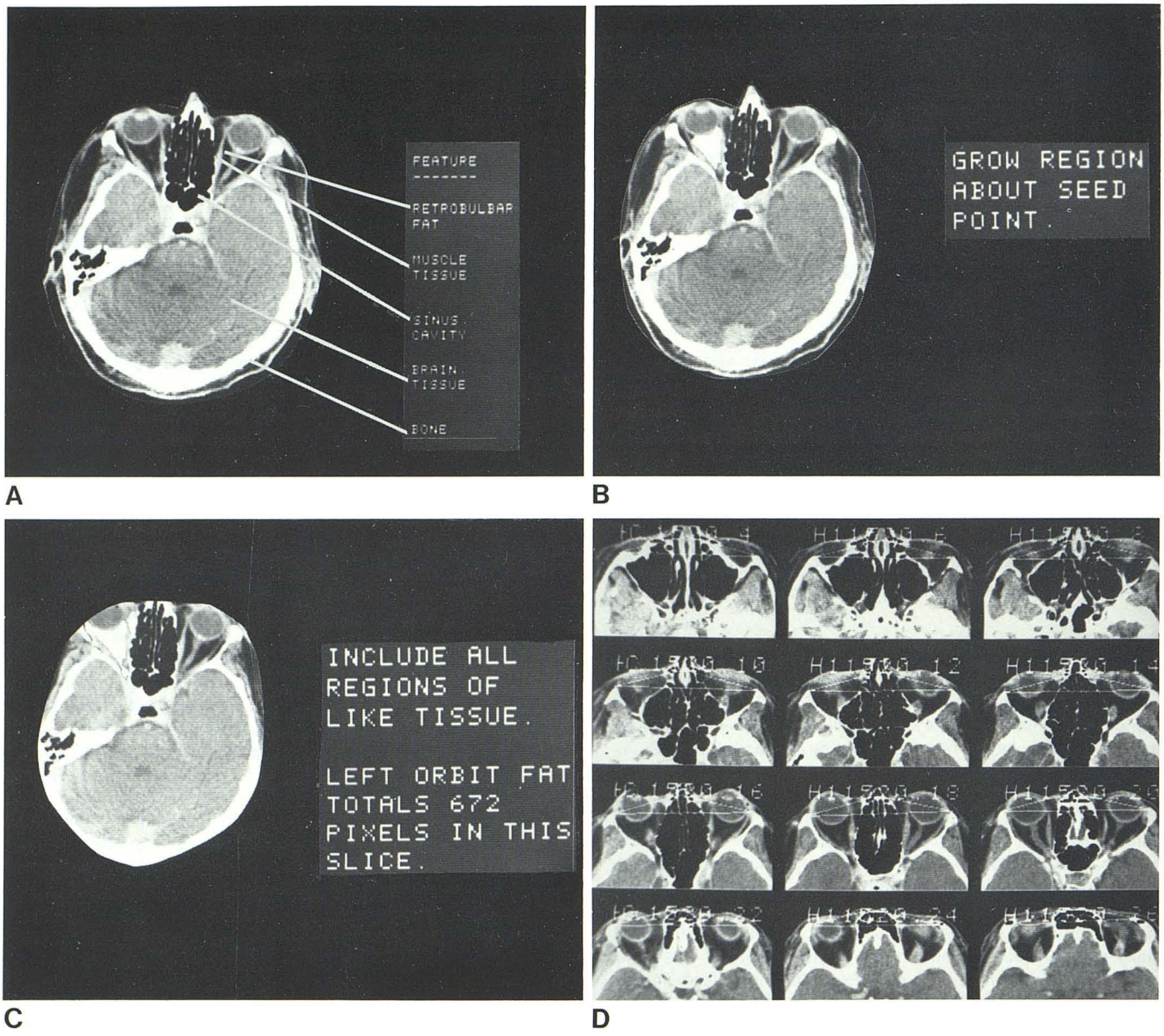

Fig. 1.—Region growing technique for volume determination. **A**, Attenuation ranges are selected for orbital structures. **B**, Program is initiated around seed point in given attenuation range. **C**, All pixels are sampled, and those falling within prescribed range are registered. **D**, Slices are summed for total pixel count within each attenuation range. Data are converted to volume measurement through pixel value calibration factor.

including 19 normal subjects and 19 patients with Graves disease. The normal patients had no history or findings of endocrine disease. Patients with Graves disease included some who were thyrotoxic with no eye changes, euthyroid with eye changes, and those with severe eye changes regardless of clinical endocrine state.

Results

The techniques showed less than 1% error in distinguishing different density structures within the large volume phantom simulating total orbit capacity. With smaller volumes, observer error and partial-volume effects became limiting factors, but errors remained below 7%.

The volume measurements in 19 normal men and women for orbital fat, muscle, fat/muscle (F/M) ratio, and total retrobulbar volume are listed in table 1. The range of values fell within 2 SD from the mean for all cases of men and women, indicating a relatively low variability about the mean. In adult women the mean volume for retrobulbar fat was 10.25 cm^3 and for orbital muscle 4.52 cm^3. In adult men the mean volume for retrobulbar fat was 11.19 cm^3 and for orbital muscle 4.79 cm^3. All patients were over the age of 15, so volume differences due to facial or orbital bone development were avoided.

The volume measurements for orbital fat, muscle, total retrobulbar volume, and F/M ratio for 19 patients with Graves disease are also listed in table 1. The general clinical category (where clearly defined) is also listed. The type A and type B classifications denote subgroups of patients who had a low F/M ratio or a normal F/M ratio, respectively, regardless of the severity of changes. Sixteen patients had muscle volumes over 2 SD above the normal mean. The other three patients demonstrated muscle volumes above the

TABLE 1: **Individual Orbital Volume Measurements with CT Analysis**

	Orbital Volumes (cm^3)			Ratio F/M	Clinical Class
	Fat	Muscle	Sum		
Normal female (n = 20):					
Range	8.82–12.20	3.66–6.20	12.70–17.30	1.42–2.96	
Mean (SD)	10.25 (1.11)	4.52 (0.68)	14.82 (1.26)	2.31 (0.36)	All I
Normal male (n = 18):					
Range	8.56–14.00	3.07–6.18	12.07–19.25	1.63–3.29	
Mean (SD)	11.19 (1.59)	4.79 (0.85)	15.98 (2.02)	2.40 (0.45)	All I
Graves type A (n = 18):					
Range	3.73–14.16	5.92–16.15	11.46–23.70	0.47–1.50	
Mean	8.05	9.09	17.14	0.96	1 II, 4 III, 4 V
Graves type B (n = 20):					
Range	8.77–20.15	4.71–9.20	13.48–29.11	1.67–2.38	
Mean	14.26	7.10	21.37	2.02	2 II, 5 III, 3 V

Note.—Clinical class: I = normal; II = hyperthyroid, no infiltrative ophthalmopathy; III = euthyroid, with ophthalmopathy; IV = hyperthyroid, with ophthalmopathy; V = other combinations of altered thyroid function or ophthalmopathy. F = fat; M = muscle.

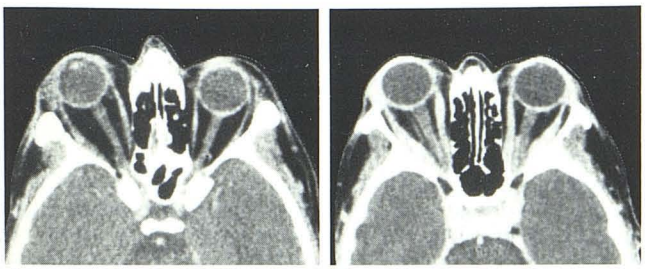

Fig. 2.—Fat and muscle volume increases in Graves disease. Increases apparent to visual observation may occur in either volume, without significant change in volume of other tissue material. **A**, Marked fat volume increase without significant muscle change. **B**, Observable muscle volume increase without significant fat volume change.

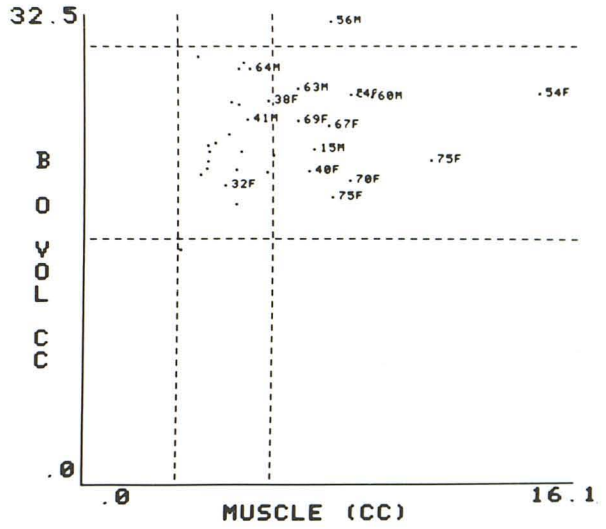

Fig. 3.—Muscle volume display (muscle volume in cm^3 × bony orbital volume in cm^3). Each unlabeled dot represents figures for normal patient within square containing normal mean ± 2 SD. Labeled dots (e.g., · 64M) place muscle volume of Graves patient with patient's age and gender. Most Graves patients fell above normal mean to 2 SD for muscle volume.

normal mean but within 2 SD. These same three patients were in the clinical group designated hyperthyroid without ophthalmopathy. Nine patients also had fat volumes greater than 2 SD above the normal mean. Nine patients had F/M ratios less than 2 SD below the normal mean. These patients comprised the type A group with low F/M ratios. Ten patients had F/M ratios within the normal range, comprising the type B group. A single patient scanned twice in 6 months demonstrated both increased clinical proptosis and increased CT muscle volume on the later scan.

Discussion

Special software programming (off-line) was developed to accurately determine the volume of small structures with high-resolution CT. Once initiated, the technique requires only moderate extra effort to process data from high-resolution studies obtained for general clinical purposes. Though we have directed our efforts toward orbital structures, the techniques could easily be modified to measure the volume of any body part.

There are only small differences in the normal ranges for retrobulbar muscle and fat volumes between adult men and women, and negligible differences in volumes between the normal right and left orbits in the same individual. In the retrobulbar region, fat makes up 70% of the orbital volume, while muscle and small neurovascular components comprise the other 30%. The normal mean volumes for retrobulbar fat were about 10–11 cm^3; for muscle, 4–5 cm^3, and for total retrobulbar volume, 15–16 cm^3. Mean F/M ratios ranged from 2 to 2.5.

Most patients with Graves disease had increased retrobulbar muscle volumes, but some had normal muscle volume even though they demonstrated exophthalmos clinically. Many with ophthalmopathy had normal fat volumes but, interestingly, many also had significant increases in total fat volume (fig. 2). The F/M ratio would tend to fall only if muscle enlargement occurred. Therefore, normal F/M ratio in the presence of severe ophthalmopathy indicated an increase in both fat and muscle volume. There appears to be a range of difference for increased retrobulbar bulk in Graves disease, with patients generally falling into two categories: In type A patients, there was an increase in muscle volume, with no change or a decrease in the fat volume (fig. 3). These patients had little or

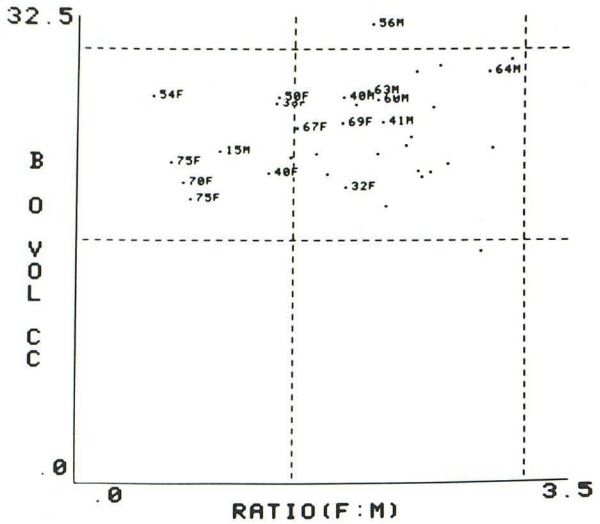

Fig. 4.—Fat/muscle volume ratio display (F/M ratio × bony orbital volume in cm^3). Labeling is identical to fig. 3. Many Graves patients remained within normal F/M ratio range despite increases in fat volume.

no overall increase in retrobulbar bulk, and little or no clinical proptosis. They were characterized by low F/M ratios with normal or only slightly increased total volumes. Type B patients had increases in both muscle and fat volume, well above normal ranges, and showed clinically the more severe signs of exophthalmos (fig. 4). These were characterized by normal F/M ratios with overall increased volumes.

Many cases have only been differentiated by specific analysis of the quantitated fat and msucle volume measurements. These changes of fat or muscle volume were often subtle in appearance on the image display, though the more extreme cases were quite apparent. Most patients with Graves disease have bilateral changes, and it is the unusual patient who has one markedly abnormal orbit and no measurable alterations in the other.

It is important to emphasize that our findings relate to changes of muscle and fat volume and not necessarily to increases in muscle or fat tissue itself. CT-quantitated increases in fat volume may be due to added fat tissue, cellular infiltration, edema, or vascular engorgement. Because the CT attenuation measurement of physical density is not sufficiently reliable, we do not believe small changes in density within a uniform tissue can be reliably correlated in different patients [13]. It is also still unclear whether a target cell or structure occurs in fat as well as muscle or if fat changes are secondary physical effects due to vascular congestion or water absorption.

Obviously, more patients must be examined in our ongoing studies so that the observed muscle and fat alterations can be more clearly correlated with clinical manifestations and therapeutic response in this generalized disease process.

REFERENCES

1. Enzmann DR, Donaldson SS, Kriss JP. Appearance of Graves' disease on orbital computed tomography. *J Comput Assist Tomogr* **1979**;3:815–819
2. Wing SD, Hunsaker JN, Anderson RE, VanDyke JL, Osborn AG. Direct sagittal computed tomography in Graves' ophthalmopathy. *J Comput Assist Tomogr* **1979**;3:820–824
3. Forbes G. Computed tomography of the orbit. *Radiol Clin North Am* **1982**;20:37–49
4. Daicker B. The histological substrate of the extraocular muscle thickening seen in dysthyroid orbitopathy. *Klin Monatsbl Augenheilkd* **1979**;174:843–847
5. Magora A, Chaco J, Zauberman H. An electromyographic investigation of ophthalmoplegia in thyrotoxicosis. *Arch Ophthalmol* **1968**;79:170–173
6. Schultz RO, Van Allen MW, Blodi FC. Endocrine ophthalmoplegia: with an electromyographic study of paretic extraocular muscles. *Arch Ophthalmol* **1960**;63:217–225
7. Breinin GM. New aspects of ophthalmoneurologic diagnosis. *Arch Ophthalmol* **1957**;58:375–388
8. Trokel SL, Jakobiec FA. Correlation of CT scanning and pathologic features of ophthalmic Graves' disease. *Ophthalmology* **1981**;88:553–564
9. Brenner DE, Whitley NO, Houk TI, Aisner J, Wiernik P, Whitley J. Volume determinations in computed tomography. *JAMA* **1982**;247:1299–1302
10. Rhodes ML. Towards fast edge detection for clinical 3-D applications of computer tomography. In: *Proceedings of the 6th Conference Comp. Appl. Rad. & Anat. Radiol. Images, Newport Beach, Calif., IEEE Society.* New York: Institute of Electric Electronic Engineers, **1979**:321–327
11. Rosenfeld A, Kak A. *Digital picture processing.* New York: Academic, **1976**
12. Keller J, Edwards M, Rundle R. Automatic outlining of regions on CT scans. *J Comput Assist Tomogr* **1981**;5:240–245
13. Levy C, Gray JE, McCullough EC, Hattery RR. The unreliability of CT numbers as absolute values. *AJR* **1982**;139:443–447