Minimization of Extraocular Muscle Damage in Thyroid Eye Disease Patients Following Surgery Based on Computerized Biomechanics

Byeong-Cheol Jeong
Department of Biomedical Engineering, Graduate School, Pusan National University

Chi-Seung Lee
Department of Convergence Medicine and Biomedical Engineering, School of Medicine, Pusan National University, and Biomedical Research Institute, Pusan National University Hospital

Dong-man Ryu
Medical Research Institute, Pusan National University

Jungyul Park (ophjyp@naver.com)
Department of Ophthalmology, School of Medicine and Biomedical Research Institute, Pusan National University Hospital

Research Article

Keywords: Thyroid Eye Disease, Orbital Decompression, Hypertrophy, Inferior Rectus Muscle, Recurrence, Finite Element Analysis

Posted Date: December 20th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-1151937/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Background

To evaluate the risk of general orbital decompression in patients with thyroid eye disease (TED).

Methods

In this study, we replicated the behavior of intraorbital tissue in patients with TED based on finite element analysis. The orbit and intraorbital tissues of TED patient who underwent orbital decompression were modeled as finite element models. The stress was examined at a specific location of the removed orbital wall of a patient with TED who had undergone orbital decompression, and its variation was investigated and analyzed as a function of the shape and dimension (to be removed).

Results

In orbital decompression surgery which removes the orbital wall in a rectangular shape, the stress at the orbital wall decreased as the width and depth of the removed orbital wall increased. In addition, the stress of the non-chamfered model (a form of general orbital decompression) was higher than that of the chamfered model. Especially, in the case of orbital decompression, it can be seen that the chamfered model compared to the non-chamfered model have the stress reduction rate from 11.08% to 97.88%.

Conclusions

It is inferred that if orbital decompression surgery considering the chamfered model is performed on an actual TED patient, it is expected that the damage to the extraocular muscle caused by the removed orbital wall will be reduced.

Background

Thyroid eye disease (TED) is an autoimmune disease characterized by lymphocyte infiltration in the orbit, including the extraocular muscle (EOM) and fat. TED has a worldwide prevalence rate of 0.1–0.3%, and it has been reported to occur in approximately 40% of patients with Graves’ disease [1–3]. As the orbital inflammation progresses, swelling of the EOM and fat, increasing intraorbital pressure (IOP), proptosis, compressive optic neuropathy, and visual loss may occur [4, 5]. Several treatment strategies are available, including high-dose glucocorticoid therapy, orbital radiation therapy, and Teprotumumab treatment, which is a novel insulin-like growth factor-1 receptor (IGF-1R) antibody [3, 6]. Surgical treatment for TED is typically a multistage approach, and 20–30% of patients are offered the option of surgery after the disease stabilizes. Orbital decompression is the first-stage approach in sequential surgical treatment and is generally performed in inactive TED patients who have severe proptosis, exposure keratopathy, facial disfigurement, persistent prolonged congestion, and high IOP [7]. When vision is threatened by compressive optic neuropathy, emergent orbital decompression may be needed, even in the active phase of TED [8]. Unfortunately, despite these treatments, there is a possibility of disease recurrence owing to various reasons such as instability of thyroid hormone, continuous smoking [9], and in some cases, orbital surgery itself, which can reactivate inflammation, exacerbate ophthalmopathy, postoperative motility disturbances, and cause the re-growth of the EOMs [5, 8, 10, 11].
In a previous study, a significant increase in medial rectus muscle volume was observed postoperatively in patients with TED who underwent orbital decompression surgery [12]. The mean volume of the inferior rectus muscle (IR) also increased after orbital decompression surgery. Some hypotheses have been suggested to explain the observed outcomes, such as the mild inflammatory reaction during surgery or the hydrostatic pressure changes that occur owing to the expanded orbital volume during surgery [12]. However, the etiologies of these postoperative volumetric changes, motility disturbances, and reactivation of the disease are still unclear [11]. To identify and solve these problems indirectly, animal experiments or finite element analysis (FEA) can be used. In particular, in silico methods using FEA have been extensively used for many years for the investigation of disease mechanisms occurring in other organs and are also extensively applied in eye-related research.

Power et al. performed an FEA of the eye damage caused by debris in a car collision, based on the results of the pig's eye and projectile collision experiment, in the same environment as the experiment [13]. The results of the experiment and FEA were consistent, and the model proved effective at simulating ocular impacts [13]. Cirovic et al. confirmed eye rotation and IOP rise owing to collision with an object and reported the results of FEA regarding damage to the eyeball and optic nerve [14]; Geng et al. performed simulations of a ball-shaped object striking the frontal bone, temporal bone, brow, and cheekbones, and the resulting absorption of the impact energy, IOP, and strains on the macula and ora-serrata were analyzed to evaluate retinal injuries [15]. In addition, Wu et al. established an optimal surgical plan according to the stress distribution applied to the eye and muscle in robot-assisted surgery, and a study was conducted to measure the stress distribution of the eyeball (based on an FEA) following the penetration of a needle in a finite element eye model [16]. Schutte et al. simulated the rotation of the eyeball and displacement of the EOM due to torsion using the FEA technique and then analyzed the intraorbital eye behavior [17].

Although these studies on the behavior of the eyeball, optic nerve, and retina have been conducted using FEA, research on surgical orbital decompression has been limited. In addition, in clinical studies, absolute standards for the location and method of orbital wall removal and the size or shape of the bone to be removed have not been quantitatively established. Thus, actual surgeries are performed depending on the experience of the clinicians.

Therefore, in this study, the behavior of the hypertrophy of the EOM, which is the main cause of the increase in IOP, was simulated using the finite element method, and an FEA technique was proposed for the analysis of the location, size, and shape of the removed orbital wall. In particular, this study focuses on the IR muscle, which is one of the most common muscles affected in TED [18], and examines the stress value of the orbital wall according to the hypertrophy of this muscle and fat. In addition, the location of the removed orbital wall was identified based on considerations of the maximum stress value, and the effects of the type and dimension of the removed orbital wall were examined.

**Methods**

**Analysis of major orbital dimensions based on magnetic resonance imaging**
In this study, the patient’s right orbit was used for comparison with the left orbit where TED occurred, and the major dimensions of both orbits were measured. As shown in Fig. 1(a), a straight line was drawn in the magnetic resonance imaging (MRI) cross-section of the patient by connecting the end points of the zygomatic bone and maxillary bone, and another straight line was formed perpendicular to this straight line, which passed through the central point of the eyeball to measure proptosis. A comparison of the proptosis dimensions of the two orbits confirmed that the proptosis in the TED orbit was 2.32 mm. As shown in Fig. 1(b), straight lines were drawn in four azimuthal directions based on the center point of the eyeball in the sagittal plane of the patient’s MRI, and a blue line was formed by connecting both ends of the lens of the eyeball. After drawing a straight line in which the generated blue line and the center of the eyeball were perpendicular to each other, the angle was measured as shown in the figure. By comparing the eye rotation dimensions of both orbits, it was confirmed that the eyeball rotation in the orbit affected by TED was rotated by 6.84°. Figure 1(c) shows a straight line perpendicular to the end point of the eyeball and a straight line perpendicular to the end point in the lower skin in the sagittal plane of the patient. The distance between the two straight lines was then measured. By comparing the two distances, it was confirmed that the skin protruded by 0.29 mm in the orbit affected by TED. It was also confirmed that the distance in the TED orbit decreased 27.36% more than the distance measured in the normal orbit. Figure 1(d) shows the thickness and width measurements of the midpoints of each EOM in the coronal plane of the patient. In the TED orbit, the thickness and width loss rates of the medial rectus muscle (MR) were, respectively, 7.5% and 5.5%, -3.6% and 0.8% in the lateral rectus muscle, and -1.59% and 1.25% in the superior rectus muscle compared with the normal orbit. Overall, the thickness of all the EOMs increased, and the width decreased in the TED orbit compared with the normal orbit. In addition, all measurements conducted in Fig. 1 were repeated five times each, and the average values for these measurements were derived, as listed in Table 1. All these dimensions were used as the criteria for selecting the load condition in a computerized analysis of IR and fat hypertrophy.

### Table 1
Dimensions measured in Fig. 1.

| Variables | A    | B    | C    | D    | E    | F    |
|-----------|------|------|------|------|------|------|
| Dimension | 14.91| 17.23| 25.97| 32.81| 1.06 | 0.77 |
| LR        |      |      |      |      |      |      |
| Normal    | 3.60 | 3.73 | 3.43 | 3.69 | 3.78 | 3.84 |
| TED       |      |      |      |      |      |      |
| MR        |      |      |      |      |      |      |
| Normal    | 8.18 | 8.11 | 9.50 | 8.97 | 7.97 | 7.87 |
| TED       |      |      |      |      |      |      |

**Modeling and material properties**

In this study, the eyeball, orbit, EOM, optic nerve, skin, and fat were all expressed as a finite element model using Mimics (version 19.0, Materialize, Leuven, Belgium), as shown in Fig. 2. In the case of the EOM, four rectus muscles were expressed, but in the case of the two oblique muscles, there was a model limitation in the expression; therefore, these were excluded. In addition, a model resembling the shape of the IR was created inside the IR, as shown in Fig. 2. This allowed the simulation of the enlarged IR. When a load condition was applied only to the inner or outer parts of the IR, the same shape as the actual hypertrophied IR could not be derived; thus, both load conditions were applied at the same time for analysis. Finally, ABAQUS (version 6.14,
Dassault Systemes, SIMULIA, USA) was used to perform three-dimensional FEA, and the finite element model consisted of a total of 901,542 solid elements.

Table 2 lists the material properties for the elastic modulus (E), Poisson's ratio (ν), and density (ρ) of each tissue applied in the FEA for patients affected with TED. The fat surrounding the eye was assumed as nearly incompressible “soft” human tissue with a ν value of 0.49 [13]. In the case of EOM, information on human material properties is lacking from existing literature. Therefore, in this study, the material property values were estimated by referring to the literature dealing with the tensile test results of the bovine EOM [13, 17], and material properties that changed owing to hypertrophy of the IR were also based on published citations in literature [19]. In the FEA, the eyeball was set as a rigid body because only the proptosis and eye rotation measurements were significant, and stress was not required. In addition, the material properties of the orbital wall, optic nerve, and skin were also investigated, as listed in Table 2, based on references in literature [14, 15].

### Table 2

| Variables     | Fat  | EOMs | Optic nerve | Orbital wall | Eye ball | Skin |
|---------------|------|------|-------------|--------------|----------|------|
| E (MPa)       | 0.047| 0.09 | 5.5         | 14500        | 14500    | 1    |
| ν             | 0.49 | 0.4  | 0.47        | 0.35         | 0.3      | 0.45 |
| ρ (kg/m³)     | 999  | 1600 | 1012        | 1610         | -        | -    |

**Boundary and load conditions**

Figure 3 shows the boundary and load conditions of the finite element model. In the boundary conditions, the orbital movement was restricted by securing the orbital outer wall, as shown in Fig. 3(a), and the degrees-of-freedom from the axial direction and rotation were restricted to the surface behind the orbital inner wall and the surface where the ocular and optic nerves begin, as shown in Fig. 3(b). As shown in Fig. 3(c), the load condition was applied at two positions, and the direction was set perpendicular to the surface of the IR. Hypertrophy was simulated by generating internal muscle pressure (IMP) on the surface of the internal IR, and by generating external muscle pressure (EMP) on the surface of the external IR. In addition, as shown in Fig. 3(d), fat pressure toward the skin (FPS), eyeball (FPE), and tissue (FPT) were generated to simulate fat hypertrophy. On average, the IOP of an adult is 3 to 6 mmHg [20]. In this study, the maximum value was set at 6 mmHg (which is equivalent to 800 Pa).

**FEA scenarios of IR muscle and fat hypertrophy**

In this study, various loading conditions were applied to simulate IR muscle and fat hypertrophy in patients affected with TED. First, by applying a load condition of 45 MPa to the EMP and 300 MPa to the IMP, IR hypertrophy was simulated. Subsequently, to simulate fat hypertrophy, first, a single load condition of 100–500 kPa (interval: 50 kPa) was applied to the FPE to simulate the fat pressure toward the eyeball. The error range was set up to +20% of the eye rotation and proptosis values measured by MRI, and it was confirmed that the results under the load condition of 100–400 kPa (interval: 50 kPa) were within the error range. Second, subject to the load condition of 100–400 kPa (interval: 50 kPa), a load of 5–15 kPa (interval: 2.5 kPa) was applied to simulate the pressure applied from fat to the eyeball and skin. Subject to the combined loading conditions of
FPE and FPS, the error range was set to ± 20% of the eyeball rotation, proptosis, and skin protrusion measured by MRI. It was confirmed that the results were within the error range subject to the load conditions of FPS 10 and 12.5 kPa at FPE 250 kPa, load conditions of FPS 5–15 kPa (interval: 2.5 kPa) at FPE 300 kPa, and load conditions of FPS 12.5 and 15 kPa at FPE 350 kPa. In the case of the FEA of the IR and fat hypertrophy, the error range was set to be wide because it is not easy to judge the analogy of the behavior according to the fat loading condition. Thereafter, FEA was performed by applying an additional load condition of 5–15 kPa (interval: 2.5 kPa) of FPT in the load conditions within the previously selected error range.

**FEA scenarios of orbital wall removal**

The maximum stress point was identified at the optimal load conditions for the IR muscle and fat hypertrophy, and the orbital wall was removed (rectangular or circular shapes), and a series FEA was performed as shown in Table 3. In the case in which the removed orbital wall was rectangular, a distance of 5 mm from the posterior surface of the orbital wall was assumed to be a risk area associated with the removal of the orbital wall. In addition, the posterior edge of the inner orbital wall was fixed at 8 mm to facilitate the removal of the rectangular orbital wall. Subsequently, the length of the front edge of the orbital wall and the depth of the rectangle to be removed were changed, and an FEA was performed according to the presence or absence of chamfering. When the shape of the removed orbital wall was circular, the maximal stress point in the IR muscle and fat hypertrophy FEA was set as the center point of the circle. Subsequently, FEA was performed according to the diameter of the circle and the presence or absence of a chamfer.

| Table 3 | Scenarios associated with orbital wall removal. |
|---------|------------------------------------------------|
| **Rectangular** | | |
| NO. | Chamfering | Width (mm) | Depth (mm) |
| 1 | X | 10 | 15 ~ 25 (Interval: 2) |
| 2 | X | 12 | 15 ~ 25 (Interval: 2) |
| 3 | X | 14 | 15 ~ 25 (Interval: 2) |
| 4 | O | 10 | 15 ~ 25 (Interval: 2) |
| 5 | O | 12 | 15 ~ 25 (Interval: 2) |
| 6 | O | 14 | 15 ~ 25 (Interval: 2) |
| **Circular** | | | |
| Chamfering | Diameter (mm) |
| 7 | X | 10 ~ 15 (Interval: 1) |
| 8 | O | 10 ~ 15 (Interval: 1) |
Results

Load condition selection and maximum stress point of orbit according to IR muscle hypertrophy

In this study, simulations were performed based on above mentioned scenarios to simulate the hypertrophy of IR and fat in patients with TED. As shown in Fig. 4(a–c), eye rotation, proptosis, skin protrusion, and muscle loss late were measured by adding the FPT 5–15 kPa (interval: 2.5 kPa) load condition within the error range of the FPE and FPS load conditions. As a result, as listed in Tables 4 and 5, it was possible to confirm the results with an error rate of 5% of the values measured in MRI in six cases. As shown in Fig. 4(d), the point of maximum stress was the same from the inferomedial orbital strut to the rear 1/3 point.

| Table 4 | Muscle loss rate in finite element analysis of inferior rectus (IR) muscle and fat hypertrophy (based on FPE of 300 kPa). |
|---------|---------------------------------------------------------------|
| **Thickness (mm)** | **LR** | **MR** | **SR** |
| **Thickness (%)** | -3.61 | -7.58 | -1.59 |
| **Width (mm)** | 7.71 | 7.71 | 7.15 |
| **Width (%)** | 0.86 | 5.58 | 1.25 |
| **FPS-12.5kPa** | **FPT 7.5 kPa** | **FPT 10kPa** | **FPT 12.5kPa** |
| **FPS-15kPa** | **FPT 10kPa** | **FPT 12.5kPa** | **FPT 15kPa** |
| **Loss rate measured by MRI** | **LR** | **MR** | **SR** |
| **Loss rate measured by MRI** | 409 | 3.14 | 0.21 | 4.57 | 3.64 | 0.65 | 5.04 | 4.14 | 1.09 | 4.47 | 4.95 | 5.42 | 3.54 | 4.04 | 4.55 | 0.56 | 1.00 | 1.45 |
Table 5
Main dimensions of IR and fat hypertrophy simulation.

| Case No. | FPE (kPa) | FPS (kPa) | FPT (kPa) | The distance difference between the eye and skin endpoint (mm) | (%) |
|----------|-----------|-----------|-----------|---------------------------------------------------------------|-----|
| 1        | 300       | 12.5      | 7.5       | 1.0319                                                        | -26.19 |
| 2        | 300       | 12.5      | 10        | 1.0324                                                        | -26.15 |
| 3        | 300       | 12.5      | 12.5      | 1.0330                                                        | -26.11 |
| 4        | 300       | 15        | 10        | 0.9709                                                        | -30.55 |
| 5        | 300       | 15        | 12.5      | 0.9714                                                        | -30.52 |
| 6        | 300       | 15        | 15        | 0.9721                                                        | -30.46 |
|          | Thickness (mm) | Width (mm) | Eye rotation (°) | Proptosis (mm) | Orbital Wall Stress (kPa) |
| 1        | 7.84      | 11.41     | 7.07(Down) | 2.22(Protend) | 117.44 |
| 2        | 7.84      | 11.41     | 7.03(Down) | 2.21(Protend) | 117.47 |
| 3        | 7.84      | 11.41     | 6.98(Down) | 2.20(Protend) | 117.50 |
| 4        | 7.84      | 11.41     | 7.16(Down) | 2.25(Protend) | 117.09 |
| 5        | 7.84      | 11.41     | 7.12(Down) | 2.24(Protend) | 117.12 |
| 6        | 7.84      | 11.41     | 7.08(Down) | 2.23(Protend) | 117.15 |

Stress distribution and trends in removing the orbital wall in a rectangular shape

In the FEA of IR and fat hypertrophy in patients with TED, the optimal loading conditions were identified. Subject to the optimal load conditions, the range was set in a rectangular shape based on the maximum stress point in the orbit wall, the orbital wall was removed, and the surrounding stress was measured. Stress was measured at the two vertices of the inner corner of the orbit, which are common in the rectangular-shaped orbital wall removal scenarios. Figure 5 shows that the stress in the FEA before and after chamfering at the left vertex does not have a significant effect, depending on the removal depth and width. However, the FEA results before and after chamfering indicated that there was a slight difference in stress.

In the case of the right vertex, as shown in Fig. 6, the stress decreased as the width and depth of the removed orbital wall increased, and the stress difference before and after chamfering was clearly identified. In addition, the analysis of the chamfered model confirmed low-stress levels, regardless of the depth and width, in most cases. Therefore, in the right vertex, it was confirmed that there was a large stress difference depending on the presence of chamfering rather than the depth or width removed, as shown in Table 6.
Table 6
Stresses at left and right measurement positions induced following the removal of the orbital wall with a rectangular shape.

| Depth (mm) | Width (mm) | Stress of left point (MPa) Before Chamfering | Stress of left point (MPa) After Chamfering | Stress of right Point (MPa) Before Chamfering | Stress of right Point (MPa) After Chamfering |
|-----------|-------------|---------------------------------------------|-------------------------------------------|---------------------------------------------|-------------------------------------------|
| 15        | 10          | 0.035326                                   | 0.03062                                   | 6.24453                                    | 0.813527                                  |
| 12        | 0.054737    |                                            |                                           | 4.13248                                    | 0.302808                                  |
| 14        | 0.04535     |                                            |                                           | 1.28819                                    | 0.259452                                  |
| 17        | 10          | 0.038368                                   | 0.03053                                   | 4.92509                                    | 0.764399                                  |
| 12        | 0.057419    |                                            |                                           | 3.02016                                    | 0.307206                                  |
| 14        | 0.038398    |                                            |                                           | 0.95818                                    | 0.284504                                  |
| 19        | 10          | 0.040739                                   | 0.03198                                   | 3.57721                                    | 0.538666                                  |
| 12        | 0.04911     |                                            |                                           | 2.79114                                    | 0.276484                                  |
| 14        | 0.041005    |                                            |                                           | 1.01248                                    | 0.241615                                  |
| 21        | 10          | 0.038983                                   | 0.03153                                   | 2.48868                                    | 0.400518                                  |
| 12        | 0.043538    |                                            |                                           | 2.16375                                    | 0.282113                                  |
| 14        | 0.044043    |                                            |                                           | 0.90297                                    | 0.238358                                  |
| 23        | 10          | 0.038903                                   | 0.03126                                   | 2.03128                                    | 0.33216                                   |
| 12        | 0.035255    |                                            |                                           | 1.89548                                    | 0.26846                                   |
| 14        | 0.090272    |                                            |                                           | 1.011                                      | 0.20817                                   |
| 25        | 10          | 0.042763                                   | 0.03394                                   | 1.621                                      | 0.300002                                  |
| 12        | 0.041728    |                                            |                                           | 1.31453                                    | 0.2928                                    |
| 14        | 0.042743    |                                            |                                           | 0.92155                                    | 0.169208                                  |

Stress distribution and trends following the removal of the orbital wall with a circular shape

In the case of circular orbital wall removal, the maximum stress point in the IR and fat hypertrophy FEA was the center point of the circle, and the orbital wall (circular shape) was removed owing to the increase in diameter before and after chamfering, and the surrounding stress of the removal position was measured. The stress measurement position was divided along four directions, as shown in Fig. 7(a), and the stress measurement was performed at three points by selecting the direction with a high-stress distribution rate. As a result, the FEA of the orbital wall removal model before chamfering, as shown in Fig. 7 (b–d), confirmed that point α had lower stress than the other points owing to the distance from the maximum hypertrophy point of the IR. In addition, in the case of the β and γ points, the stress tends to decrease as the length of the diameter increases. Accordingly, it was confirmed that the high stress was measured when the diameter of the removed orbital wall was 11 mm.
As shown in Fig. 8, when the IR is hypertrophic, the positions of the $\beta$ and $\gamma$ points, when the removed orbital wall is 11 mm in diameter, coincide with the point of maximum hypertrophy of the IR, and it is considered that the load of the highest stress is received. In the case of the models with diameters in the range of 10–15 mm the load applied to the $\beta$ and $\gamma$ points was reduced as the diameter decreased or increased based on the diameter of 11 mm. Therefore, it was confirmed that the stress of the IR was highest near the maximum hypertrophy point of the IR in the case of the $\beta$ and $\gamma$ points. In addition, in the analysis of the chamfered orbital wall removal model, it was confirmed that the stress was lower than the stress in the analysis of the model before chamfering at all points of $\alpha$, $\beta$, and $\gamma$, as shown in Table 7.

| Diameter (mm) | Stress of $\alpha$ point (MPa) | Stress of $\beta$ Point (MPa) | Stress of $\gamma$ Point (MPa) |
|---------------|-------------------------------|-------------------------------|-------------------------------|
|               | Before Chamfering | After Chamfering | Before Chamfering | After Chamfering | Before Chamfering | After Chamfering |
| 10            | 0.528024          | 0.1746           | 6.536398         | 0.516669         | 6.935254         | 0.207131         |
| 11            | 0.459065          | 0.159243         | 9.551042         | 0.287233         | 8.859715         | 0.187805         |
| 12            | 0.567837          | 0.035651         | 3.12807          | 0.134126         | 7.912384         | 0.370978         |
| 13            | 0.58731           | 0.114341         | 0.41591          | 0.2646           | 6.40473          | 0.649128         |
| 14            | 0.554781          | 0.150457         | 0.945533         | 0.277382         | 4.206018         | 0.507885         |
| 15            | 0.71653           | 0.064393         | 0.37459          | 0.23486          | 1.42209          | 0.761282         |

Computed tomographic analysis of patient datasets with orbital wall removed

In this study, we analyzed the computed tomography (CT) scans of TED patients who underwent orbital decompression to understand the risk of recurrence of TED. Figure 9 shows the orbital and intraorbital tissues of four patients whose orbital floor and orbital medial wall had been removed previously, based on the sagittal and transverse plane CT scans. The analysis of Fig. 9 was conducted first. When confirmed by MRI, as shown in Fig. 9, the margin and EOM of the surgical site with a steeply inclined surface were observed. This EOM was hypertrophied, the amount of bone (proximal to this muscle) removed was large, and the larger the release of volume through the decompression site, the greater the contact between muscle and bone. Moreover, when the orbital medial wall was removed, as shown in Fig. 9(b), it was confirmed that it appeared more prominently. After orbital decompression, it was confirmed that the margin and EOM of the bone were adjacent to the maximum stress point, and that a large extrovert change in the EOM and stress force occurred.

Discussion

TED is a disease in which the eyeball protrudes forward owing to an increase in IOP attributed to EOM and fat hypertrophy. Accordingly, orbital decompression is required to remove the orbit wall and lower the IOP. In this study, the IR and fat hypertrophy of patients with TED were simulated, and the maximum stress point of the orbital wall was identified. Subsequently, FEA was performed by removing the orbital wall based on the
maximum stress point of the orbital wall according to the shape and size. The stress around the removed orbital wall was measured to confirm the change in stress according to the shape and size.

First, in this study, we analyzed the MRI of patients with TED and constructed a three-dimensional finite element model; in the case of IR, the IR model before hypertrophy was implemented by analyzing the dimension of the IR in the patient's normal orbit. In addition, a model similar to the shape of the IR was created inside it to show the hypertrophic response of the IR muscle. When the load value was defined only inside or outside the IR muscle, the shape as the actual hypertrophic IR muscle cannot be reproduced; thus, the two load values were applied simultaneously. In the cases in which only the IR muscle was hypertrophic, the eye rotation and proptosis could not be measured; therefore, the load condition was given in the vertical direction of all the surfaces associated with the fat, and the fat hypertrophy was simulated. According to the results of simulating the IR and fat hypertrophy, it was confirmed that the thickness and width of the IR muscle, proptosis, eye rotation, distance from the skin and the end point of the eyeball, and the muscle's loss rate were associated with an error rate of ±5% according to the dimension measured on MRI. In addition, in the case of the maximum stress point on the orbital wall owing to IR and fat hypertrophy, it was determined to be the location where surgery was performed clinically. Based on these results, it is considered that the FEA of IR and fat hypertrophy performed in this study is reliable.

In the FEA of the IR and fat hypertrophy, orbital decompression was simulated by removing the orbital wall in a rectangular shape based on the maximum stress point. In this case, removal was not performed, as a distance of 5 mm anterior from the posterior surface of the orbital inner wall was assumed as a risk area for orbital wall removal. This was established because when removal was attempted at the back of the orbital lining, increasing the risk of tissue damage, it was difficult to access the end clinically. In addition, to evaluate the stress trend according to the removed depth and width, the stress at the inner vertex was measured in the nonchamfered model, and the stress in the middle of the edge connected to the inner vertex in the chamfered model was also assessed. This was set as the stress measurement location because it is the only location that is the same even if the depth and width of the orbital wall to be removed in the rectangular orbital decompression FEA changed. As a result of the measurement of the right vertex stress in the rectangular orbital decompression FEA, it was observed that the load decreased as the values of the removed depth and width increased, and it was confirmed that a large load stress was applied to the right vertex in the analysis before chamfering compared with the post-chamfering state. However, in the case of the left vertex, there was no significant difference in stress according to the values of depth and width, and it was confirmed that similar stress was applied to the difference in stress before and after chamfering. It is thought that this is because the load transmission was weakened as the position of the hypertrophic IR was farther away.

Additionally, in the FEA of the IR and fat hypertrophy, orbital decompression was simulated in which the maximum stress point was set to the distal center and the orbital medial wall was removed in a circular shape. In the case of orbital decompression in the case in which a circular part of the wall was removed, four orientations were set in the circle, and three points were selected in the area where the highest stress was generated to measure the stress. This was established because the removed circle became larger as the diameter length increased. Thus, it was not possible to measure the stress at the same location as in the rectangular orbital decompression procedure. In the case of position α, as the distance from the hypertrophic IR increased, the load applied to this position decreased, and a low-stress level was measured, and the difference
in stress before and after chamfering was insignificant. In the case of the β and γ points, the load tended to
decrease as the diameter increased. This was because it coincided with the point of maximal IR hypertrophy.
Consequently, it was proved that when the diameter of the removed circle decreased or increased by more than
11 mm, it moved away from the point of maximum hypertrophy of the IR and resulted in low-load stress values
at the β and γ points. However, in the cases of the β and γ points after chamfering, there was no decrease in the
stress of the orbital wall according to the increase in diameter. These findings confirmed that the stress bands
were similar. As a result, it was confirmed that the nonchamfered model was significantly affected by the
hypertrophic IR muscle compared to the chamfered model, regardless of the shape of the removed orbital wall.

In addition, in this study, we analyzed the CT images of TED patients who underwent orbital decompression to
understand the risk of recurrence of TED. The removed margin of the orbital medial wall and margin of the
orbital floor had a steep slope, and it was confirmed that they were in close contact with the EOMs. Hu et al.
reported that the volume of IR and MR increased after orbital decompression surgery [12]. Therefore, in this
study, it was judged that inflammation was generated in IR and MR owing to the close contact between the bone
edge and muscle, which is one of the causes of TED recurrence. There is a need for a method to minimize EOM
damage to prevent TED recurrence, and a method to minimize damage because there is concern about large
damages to the EOM when TED recurs.

In this study, in the case of the nonchamfered orbit model, the shape of the bone margin removed during orbital
decompression in actual surgery was similar. As a result of simulation of the orbital decompression through
FEA, a large stress was confirmed in the nonchamfered orbital wall. Therefore, we reaffirmed the concern that
the EOM would be severely damaged by sharp edges. As a first method to minimize EOM damage, chamfered
orbital decompression is proposed. It was confirmed that in the case of chamfered orbital decompression
proposed according to FEA, the stress applied to the orbital wall was significantly reduced compared with
nonchamfered orbital decompression. Therefore, when implementing actual orbital decompression and
chamfering by drilling, the stress applied to the EOM is reduced, and the damage is minimized. However, there
are cases wherein it is difficult to implement chamfering because the thickness of the orbital wall is low. In this
case, another method is required to protect the sharp edges of the margin.

Therefore, in this study, we provide a method of incising the periorbita between the orbital wall and fat in a
specific form by the second method. Periorbita exists between the orbital wall and fat; however if this periorbita
is not removed, there will not come out fat and EOM even if the orbital wall is removed. Various things are
reported in the paper on periorbita incision. The method of removing the orbital wall and then completely
removing the periorbita [4, 21], the method of ‘The orbital sling procedure’ to keep some periorbita on the medial
rectus muscle intact [22], and the method of making a parallel incision of the periorbita from the posterior to the
anterior is being reported [23, 24]. If you perform the method of completely removing periorbita and the method
of orbital sling procedure, periorbita does not protect the edge of the removed orbital wall and can cause
damage to the EOM. In this study, we propose a method in which the periorbita is incised in the shape of 'II' in
parallel from the posterior to the anterior direction, and incisions are made in the direction perpendicular to the
incised line to perform the incision in the shape of 'H'. Therefore, if the orbital wall is removed and the periorbita
existing between the orbital wall and fat is incised in an “H” shape, it is thought that the periorbita will be
attached to the removed orbital wall to cover the sharp edge and minimize the damage to the EOM.
However, this study had several limitations. First, two oblique muscles existed in addition to the four EOMs among all the muscles inside the orbit, and various biological tissues, such as ligaments, were configured inside the orbit. Various biological tissues, such as oblique muscles and ligaments, were excluded from this analysis because the location and exact dimensions could not be determined from the MRI and CT data. It is believed that more accurate results can be obtained if the oblique muscle can be simulated. However, even if the oblique muscles were excluded, it is judged that it is fine to omit them because the behavior inside the orbit of a patient with TED can be simulated with four EOMs. In addition, the material properties of the finite element model of the orbit and intraorbital tissues were assumed based on animal experiments because of the lack of experimental literature and information on human properties. Therefore, it is thought that the accuracy of the FEA results will be further improved if only the human material properties can be secured. However, there are ethical issues associated with the conduct of in vivo experiments. Therefore, in this study, the physical properties of the orbit and intraorbital tissues were applied using the results of published animal experimental studies.

**Conclusions**

In this study, we simulated the orbit and intraorbital tissue of TED patients in which the IR muscle was enlarged with a finite element model, and an FEA was performed to assess the responses of tissues in the orbit of patients affected with TED, based on the application of a load condition to the IR muscle and fat. Thereafter, an FEA of the tissue behavior in the orbit of a patient affected with TED was performed after the removal around the point of maximum stress on the orbital lining under the same conditions, and the stress of the orbital wall at a specific point was measured according to the shape and location of the removed orbital wall. Therefore, the main conclusions of this study are as follows.

- The hypertrophic load conditions of the IR muscle alone could not simulate the rotation and extrusion of the eye, and the addition of fat hypertrophy load conditions could simulate the intraocular tissue behavior of patients with TED.
- The maximum stress point of the orbital wall was identified by the FEA of the IR and fat hypertrophy, and this point was applicable to surgery.
- When the removed orbital wall had a rectangular shape, the difference in stress before and after chamfering was small at locations farther than the IR hypertrophy position. However, nonchamfered model analysis at a point close to the IR hypertrophy position confirmed that the stress applied to the orbital wall decreased as the depth and width of the removal increased.
- In the case of the chamfered model analysis, in the instances in which the removed orbital wall had a rectangular shape, it was confirmed that even though the stress decreased as the overall removal depth and width increased, the stress width was not large. In addition, it was confirmed that the orbital wall stress of the nonchamfered model, which was a form of general orbital decompression, formed a larger load than the stress of the orbital wall of the chamfered model.
- In the case of the nonchamfered model, in the instances in which the removed orbital wall had a circular shape, it was confirmed that the stress of the orbital wall decreased as the diameter increased, but the highest stress was measured at a specific diameter. This was because stress measurement position at a specific diameter was close to the maximum IR hypertrophy point. In the case of the chamfered model,
there was no difference in stress according to the diameter of the removed circle, and the stress was found to be similar.

- When the removed orbital wall had a circular shape, it was confirmed that the stress of the nonchamfered model, which had a form of general orbital decompression, was significantly greater than the stress of the orbital wall of the chamfered model.

- Therefore, it was confirmed that the edge of the removed orbital wall, regardless of the removal type, generated a significantly higher stress on the orbital wall in the case of the nonchamfered model (a form of general orbital decompression) compared with the case of the chamfered model.

- Finally, to prevent recurrence by minimizing damage to the EOM after orbital decompression and to prevent further damage to the EOM when TED recurs, if the edge of the orbital wall removed during orbital decompression was removed in a chamfering form, the EOM damage was expected to be minimal. If the thickness of the orbital wall was thin and could not be removed in a chamfering form, it is expected that the periorbita between the orbital wall and the fat could be sectioned in an “H” shape, and the orbital wall of the sharp edge would be wrapped with the periorbita to prevent damage to the EOM.

Based on the results of this study, if orbital decompression surgery is performed on an actual patient affected by TED, it is expected that the damage to the EOM caused by the removed orbital wall will be reduced. In addition, even if TED recurs, damage to the EOM can be minimized. Overall, the findings and inferences of this study are expected to be helpful in the treatment of TED in patients.

### Abbreviations

FEA: Finite element analysis; TED: Thyroid eye disease; EOM: Extraocular muscle; IOP: Intraorbital pressure; IGF-1R: Insulin-like growth factor-1 receptor; MRI: Magnetic resonance imaging; CT: Computed tomography; IR: Inferior rectus muscle; MR: Medial rectus muscle; LR: Lateral rectus muscle; SR: Superior rectus muscle; IMP: Internal muscle pressure; EMP: External muscle pressure; FPS: Fat pressure toward the skin; FPE: Fat pressure toward the eyeball; FPT: Fat pressure toward the tissue

### Declarations

#### Acknowledgements

Not applicable

#### Funding

This study was supported by Biomedical Research Institute Grant (202000150001), Pusan National University Hospital.

#### Availability of data and materials

The datasets obtained and/or analyzed during the current study are available from the corresponding author on reasonable request.

#### Author’s contributions
conception and design of the study (BCJ, CSL, DMR, JYP); Conduction of study (BCJ, DMR, JYP); Collection and management of data (BCJ, DMR, JYP); Data analysis (BCJ, DMR, JYP); Data interpretation (BCJ, DMR, JYP); Preparation, review, and approval of the manuscript (BCJ, DMR, JYP).

Ethics approval and consent to participate

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board of Pusan National University Hospital (IRB No. 2104-018-102).

Consent for publication

Owing to the retrospective nature of the study, the IRB waived the need for patient consent.

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

1Dept. of Biomedical Engineering, Graduate School, Pusan National University, Busan, Republic of Korea. 2Dept. of Convergence Medicine and Biomedical Engineering, School of Medicine, Pusan National University, and Biomedical Research Institute, Pusan National University Hospital, Busan, Republic of Korea. 3Medical Research Institute, Pusan National University, Busan, Republic of Korea. 4Dept. of Ophthalmology, School of Medicine and Biomedical Research Institute, Pusan National University Hospital, Busan, Republic of Korea.

References

1. Noth D, Gebauer M, Müller B, Bürgi U, Diem P. Graves’ Ophthalmopathy: Natural History and Treatment Outcomes. Swiss Medical Weekly. 2001;131:603–609.
2. Bartalena L, Tanda ML. Graves’ Ophthalmopathy. The New England Journal of Medicine. 2009;360:994–1001.
3. Mohyi M, Smith TJ. IGF1 receptor and thyroid-associated ophthalmopathy. J Mol Endocrinol. 2018;61:29–43.
4. Jefferis JM, Jones RK, Currie ZI, Tan JH, Salvi SM. Orbital decompression for TED: methods, outcomes, and complications. Eye (Lond). 2018;32(3):626–636.
5. Fichter N, Guthoff RF, Schittkowski MP. Orbital decompression in TED. ISRN Ophthalmol. 2012;2012:739236.
6. Bartalena L, Marocci C, Bogazzi F, Bruno-Bossio G, Pinchera A. Glucocorticoid Therapy of Graves’ Ophthalmopathy. Experimental and Clinical Endocrinology & Diabetes. 1991;97:320–327.
7. Ismailova DS, Belovalova IM, Grusha YO, Sviridenko NY. Orbital decompression in the system of treatment for complicated TED: case report and literature review. Int Med Case Rep J. 2018;11:243–249.
8. Wang Y, Patel A, Douglas RS. Thyroid Eye Disease: How A Novel Therapy May Change The Treatment Paradigm. Ther Clin Risk Manag. 2019;15:1305–1318.

9. Genere N, Stan MN. Current and Emerging Treatment Strategies for Graves' Orbitopathy. Drugs. 2019;79(2):109–124.

10. Alsuhaibani AH, Carter KD, Policeni B, Nerad JA. Effect of orbital bony decompression for Graves’ orbitopathy on the volume of EOMs. Br J Ophthalmol. 2011;95(9):1255–1258.

11. Wenz R, Levine MR, Puttermann A, Bersani T, Feldman K. EOM Enlargement After Orbital Decompression for Graves’ Ophthalmopathy. Ophthalmic Plastic and Reconstructive Surgery. 1994;10:34–41

12. Hu WD, Annunziata CC, Chokthaweesak W, Korn BS, Levi L, Granet DB, et al. Radiographic analysis of EOM volumetric changes in thyroid-related orbitopathy following orbital decompression. Ophthalmic Plast Reconstr Surg. 2010;26(1):1–6.

13. Power ED, Stitzel JD, Duma SM, Herring IP, West RL. Investigation of Ocular Injuries from High Velocity Objects in an Automobile Collision. SAE International. 2002;111:211–218.

14. Cirovic S, Bholia RM, Hose DR, Howard IC, Lawford PV, Marr JE, et al. Computer modelling study of the mechanism of optic nerve injury in blunt trauma. Br J Ophthalmol. 2006;90(6):778–783.

15. Geng X, Liu X, Wei W, Wang Y, Wang L, Chen K, et al. Mechanical Evaluation of Retinal Damage Associated With Blunt Craniomaxillofacial Trauma: A Simulation Analysis. Transl Vis Sci Technol. 2018;7(3):16.

16. Wu J, Nasseri MA, Eder M, Gavaldon MA, Lohmann CP, Knoll A. The 3D Eyeball FEA Model with Needle Rotation. APCBEE Procedia. 2013;7:4–10.

17. Schutte S, van den Bedem SP, van Keulen F, van der Helm FC, Simonsz HJ. A finite-element analysis model of orbital biomechanics. Vision Res. 2006;46(11):1724–1731.

18. Yoo L, Kim H, Gupta V, Demer JL. Quasilinear viscoelastic behavior of bovine EOM tissue. Invest Ophthalmol Vis Sci. 2009;50(8):3721–3728.

19. Barin FR, de Sousa Neto IV, Vieira Ramos G, Szojka A, Ruivo AL, Anflor CTM, et al. Calcaneal Tendon Plasticity Following Gastrocnemius Muscle Injury in Rat. Front Physiol. 2019;10:1098.

20. Kratky V, Hurwitz JJ, Avram DR. Orbital Compartment Syndrome. Direct Measurement of Orbital Tissue Pressure: 1. Technique. Canadian Journal of Ophthalmology. 1990;25:293–297.

21. Cubuk MO, Konuk O, Unal M. Orbital decompression surgery for the treatment of Graves’ ophthalmopathy: comparison of different techniques and long-term results. Int J Ophthalmol. 2018;11(8):1363–1370.

22. Metson R, Samaha M. Reduction of Diplopia Following Endoscopic Orbital Decompression: The Orbital Sling Technique. The Laryngoscope. 2002;112(10):1753–1757.

23. Jimenez-Chobillon MA, Lopez-Oliver RD. Transnasal endoscopic approach in the treatment of Graves ophthalmopathy: the value of a medial periorbital strip. Eur Ann Otorhinolaryngol Head Neck Dis. 2010;127(3):97–103.

24. Hernandez-Garcia E, San-Roman JJ, Gonzalez R, Nogueira A, Genol I, Stoica B, et al. Balanced (endoscopic medial and transcutaneous lateral) orbital decompression in Graves' orbitopathy. Acta Otolaryngol. 2017;137(11):1183–1187.

Figures
Figure 1

Analysis of major dimensions in the thyroid-eye disease (TED) orbit and normal orbit based on magnetic resonance imaging (MRI). (a) Proptosis measurement. (b) Eye rotation measurement. (c) Distance measurement between the ocular end point and the skin end point. (d) Thickness and width measurements in the extraocular muscle (EOM) except for the inferior rectus (IR) muscle.

Figure 2

Finite element model of orbit and intraorbital tissue.

Figure 3

Boundary and load conditions of finite element model.

Figure 4

Results from finite element analysis (FEA) of IR muscle and fat hypertrophy (a) Eye rotation responses according to the load conditions of fat pressure toward the skin eyeball (FPE), skin (FPS), and tissue (FPT). (b) Proptosis according to the load conditions of FPE, FPS, and FPT, and (c) distances between the ocular end point and the skin end point according to the load conditions of FPE, FPS, and FPT. (d) Maximum stress point in the IR and fat hypertrophy FEA.

Figure 5

Stress measurement position and stress graph in the left vertex following the removal of the orbital wall with a rectangular shape.

Figure 6

Stress measurement position and stress graph in the right vertex following the removal of the orbital wall with a rectangular shape.

Figure 7
Stress measurement position and stress graphs associated with the removal of the orbital wall with a circular shape. (a) Stress measurement position. (b) Stresses at positions γ, (c) α, and (d) β.

Figure 8

Behavior associated with IR hypertrophy in FEA following the removal of the orbital wall with a circular shape of diameter 11 mm.

Figure 9

CT analysis of TED patients who underwent orbital decompression surgeries.