SHORT COMMUNICATION

Diffusion tensor imaging reveals morphological alterations of the lateral pterygoid muscle in patients with mandibular asymmetry

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Objectives: To evaluate non-invasively the morphological features of both lateral pterygoid muscle (LPM) and masseter muscle by using diffusion tensor Imaging on two patients affected by mandibular asymmetry.

Methods: Two female patients with mandibular excess and asymmetry who underwent Le Fort I osteotomy and bilateral sagittal split osteotomy were recruited for this study. Morphological (T_1 weighted) and diffusion weighted images were acquired with a 3T scanner 1 week before (T0) and 1 month after the surgery (T1). Probabilistic tensor-based tractography reconstruction of bilateral masseters and LPMs was performed and mean fractional anisotropy (FA) values for both muscles were extracted.

Results: Diffusion tensor imaging was able to identify the muscle geometrical morphology and diffusion microstructural changes. Both at T0 and T1, mean FA values had no significant differences between the right and left side of masseter (at T0: $p = 0.91$; at T1: $p = 0.54$) and LPM (at T0: $p = 0.92$; at T1: $p = 0.43$), respectively. Both patients reported a significant improvement in FA mean values of the left LPM ($p = 0.03$) between T0 and T1, whereas no diffusion parameters' changes were observed for the bilateral masseter muscles and right LPM.

Conclusions: We found that after the surgery the LPM ipsilateral to the deviation side showed a significant increase of FA compared to the baseline. Although preliminary, our findings suggest that diffusion tensor imaging may represent a promising tool to investigate non-invasively the masticatory muscles in temporomandibular joint disorders.

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Introduction

Diffusion weighted imaging (DWI) provides a fascinating synthesis of study between the microscopic motion of water molecules, the gross anatomy and the variations of water diffusion in pathological conditions. The latest development of DWI is represented by diffusion tensor imaging (DTI), a technique able to make clear not only the entity but also the direction of diffusion of water molecules in tissues. The combination

of DTI together with the application of algorithms allowed for the development of fiber tracking and three-dimensional visualization of tissue orientation and course. Although DTI and tractography represent an important area of research in the evaluation of the central nervous system,¹⁻³ their applications in the field of musculoskeletal imaging and diseases is rapidly growing, proving to be able to provide muscular microstructural parameters—such as fractional anisotropy (FA) and mean diffusivity—and a good representation of muscle architecture, orientation and shape.⁴⁻⁷ Indeed,

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it is well known that the self-diffusion coefficient of water in skeletal muscle fibers is lower than the value for free water. This is likely to be due to several reasons such as the action of the myofibrils and other intracellular solid phase proteins as physical barriers to water translation; the finite permeability of the cell membrane to water; and the binding of water to solid-phase macromolecules, dissolved macromolecules and ions with smaller diffusion coefficients than that for free water.

The majority of studies assessing muscle characteristics has been conducted on lower limb (*e.g.* sartorius, hamstrings, vastus lateralis and medialis, gastrocnemius, soleus, tibialis anterioris)⁸ and extraocular muscles.⁹ In addition, DTI has been successfully used to evaluate the diffusivity properties and microstructure changes of muscular tissues in skeleton muscle injury,⁹ after exercise and to assess the effect of blood flow obstruction and re-perfusion.⁶

Shiraishi *et al*⁵ evaluated diffusion parameters of the masseter muscle at three different locations (at the level of the mandibular notch, at the level of the mandibular foramen and at the root apex of the mandibular molars) during jaw opening, clenching and rest in healthy humans, showing that diffusion parameters differed at different levels of the muscle and during different jaw positions. In particular, it has been found that apparent diffusion coefficient, the primary (λ_1), secondary (λ_2), and tertiary eigenvalues (λ_3) significantly increased bilaterally by clenching, whereas the relative distribution of the bite forces had no effect on any of the indices.^{5,10}

More recently, Liu *et al*⁴ performed *in vivo* morphological and functional evaluation of the lateral pterygoid muscle (LPM) by mean of DTI reinforcing the idea of DTI as a promising technique to study the masticatory muscles in humans *in-vivo* and non-invasively, which may potentially lead to a better evaluation of patients with temporomandibular joint disorders (TMJD) and to realize more accurate pre-surgical plans.

However, to the best of our knowledge, there is so far no study investigating the diffusion parameters changes of the masticatory muscle in patients with TMJD.

Here in, we explore the feasibility and utility of DTI in the non-invasive evaluation of both LPMs and masseter muscles reporting the cases of two patients affected by mandibular asymmetry.

Experiments and results

Two female patients with mandibular excess and asymmetry were studied in the present study. Both patients had homogeneous characteristics: (i) gender: female; (ii) age: 24 years; (iii) dento maxillofacial skeletal mandibular asymmetry: asymmetry with 4-mm lateral mandibular deviation on the left with cross-bite occlusion and class III malocclusion; (iv) no pre-surgical orthodontic treatment (v) type of surgical treatment: orthognathic “surgery first” technique.

Surgery was planned according to a computer-aided simulation program (Dolphin Imaging 11.8 computer software) and to the cephalometric program.

A Le Fort I osteotomy and bilateral sagittal split osteotomy (BSSO) were performed in both patients with a 3-mm maxillary advancement and mandibular translation in I class position. Maxilla was fixed with two L-shaped plates for each side. Mandible was fixed with bicortical lag screws. The patients underwent a MRI examination with a 3.0 T MRI scanner (Achieva, Philips Healthcare, Best, Netherlands) at IRCCS Centro Neurolesi “Bonino Pulejo”, by using a 32-channel sensitivity encoding head coil.

Morphological and diffusion MRI examination were performed 1 week before (T0) and 1 month after surgery (T1), focusing the attention on the morphological pattern of lateral pterygoid and masseter muscles of both sides.

Diffusion MRI was acquired with single-shot, diffusion weighted EPI sequence using 32 gradient diffusion directions chosen following an electrostatic repulsion model with b-value of 0 and 600 s mm⁻². The other sequence parameters were repetition time (TR) = 22.557 ms; echo time (TE) = 61 ms; field of view = FOV 240 × 240 mm²; reconstruction matrix = 120 × 120; flip angle = 90°; voxelsize = 2 × 2 × 2 mm³; axial slice thickness = 2 mm and no inter-slice gap.

To specify the regions of interest for the selected muscles, a three-dimensional high-resolution T₁ weighted fast field echo sequence was acquired using the following parameters: TR = 8.13 ms; TE = 3.7 ms; flip angle = 8°; FOV = 240 × 240 mm²; reconstruction matrix = 240 × 240; voxelsize = 1 × 1 × 1 mm³ and slice thickness = 1 mm.

Both DWI and T1W sequences were acquired with the subjects lying down on the examining table, placed feet first in a supine postural position, in which the angle between the floor and the Frankfort horizontal plane was 90°.⁴

Technical MRI sequences parameters are reported in Table 1.

In order to reduce noise and increase the signal-to-noise ratio (SNR), diffusion weighted images were pre-processed by using the local principal component analysis filter available in the Matlab DWI denoising package (<https://sites.google.com/site/pierrickcoupe/>)

Table 1 Technical parameters and pulse sequences

	<i>Diffusion</i>	<i>T₁ weighted</i>
Repetition time	22.557 ms	8.13 ms
Echo time	61 ms	3.7 ms
Field of view	240 × 240 mm ²	240 × 240 mm ²
Reconstruction matrix	120 × 120	240 × 240
Flip angle	90°	8°
Axial slice thickness	2 mm	1 mm
Voxel size	2 × 2 × 2 mm ³	1 × 1 × 1 mm ³

[softwares/denoising-for-medical-imaging/dwi-denoising/dwi-denoising-software](#)). The quality of the DWIs was visually inspected for motion, which was corrected and modelled by a rigid transformation. Eddy currents distortion artefacts were modelled as an affine transformation using the FMRIB Software Library [FSL] (www.fmrib.ox.ac.uk). The B0 image was taken as the reference image and each DW volume was aligned to it using a 12-parameters affine transformation. Rotational part of transformations was later applied to individual gradient directions too.

Tensor computation to obtain FA maps was carried out by using the FSL's DTIFIT tool. Structural T1 and corrected DWIs were co-registered by the FSL linear and non-linear registration tools (FLIRT and FNIRT). Co-registered T1W-fast field echo images were superimposed on B0 images in order to perform an accurate manual segmentation of the bilateral LPMs and masseter muscles. During this step, aponeurosis, fascia and blood vessels were avoided from regions of interest drawing. Probabilistic tensor-based tractography reconstruction of the masseters and LPMs (Figure 1) was performed by using the MRtrix software (<http://www.mrtrix.org>). Once tractography was performed, we extracted the mean FA values for both the muscles of interest. The paired *t*-test was applied to evaluate the symmetry between the right and left mean FA values as well as the differences between T0 and T1. A *p*-value of <0.05 was taken as the level of significance.

Clinically, both patients reported improved mandibular excursion in combination with an obvious improvement of their life quality.

DTI was able to identify the muscle geometrical morphology and diffusion microstructural changes.

Both at T0 and T1, mean FA values had no significant difference between the right and left side of masseter (at T0: *p* = 0.91; at T1: *p* = 0.54) and LPM (at T0: *p* = 0.92; at T1: *p* = 0.43), respectively.

Both patients reported a significant improvement in FA mean values of the left LPM (*p* = 0.03) between T0 and T1, whereas no diffusion parameters' changes were observed for the bilateral masseter muscles and right LPM (Table 2).

Discussion

During the last decades, DTI has been shown to be a feasible technique to obtain detailed information on muscle architecture both in healthy and pathological conditions. Here in, we further evaluated the application of DTI and its usefulness in the assessment of outcomes in two patients with mandibular asymmetry who underwent maxillo-facial surgery. Class III malocclusion consists of a deviation in the sagittal relationship between maxilla and mandible leading to deficiency (backward position of the maxilla) or by prognathism (forward position of the mandible). Skeletal class III is characterized by lower incidence than other sagittal disharmonies, ranging from 1 to 5%.^{11,12}

Facial asymmetries are very common features of Class III malocclusion, usually involving morphologic variation together with deviations of mandible or of the entire maxillo-mandibular complex.¹³

Figure 1 3D representations of axial views of fibers of LPMs coloured according to their principal direction. Red colour indicates a left-right direction, green colour an anteroposterior direction and blue colour a caudal-cranial direction. LPM, lateral pterygoid muscle.

Table 2 Differences of mean FA values of both right and left masseter and lateral pterygoid muscles at T0 and T1

	<i>Muscle of interest</i>	<i>T0</i>	<i>T1</i>	<i>p-value</i>
Right	Masseter	0.39	0.40	0.24
		0.47	0.50	
	Lateral pterygoid	0.30	0.31	0.38
		0.43	0.49	
Left	Masseter	0.47	0.49	0.34
		0.41	0.49	
	Lateral pterygoid	0.36	0.46	0.03*
		0.38	0.50	

*Statistical significance <0.05.

In the present pilot study we evaluated two female patients suffering from mandibular asymmetry who underwent BSSO. Although both the patients reported enhanced quality of life and clinical outcomes, a quantitative assessment of the structural changes of the muscle betrayed by the surgical treatment is needed to understand how the mandible repositioning affects function and shape of masseters and LPMs. Indeed, the surgical treatment of the lateral deviation of the mandible is likely to influence masticatory muscles such as LPMs and masseters. LPM is physiologically involved in the translation phase during jaw opening together with lateral excursion of the mandible.¹⁴ We found that mandible repositioning led to an improved mandibular excursion in translational movements which involved a facilitated chewing process. Interestingly, we found significant increase of the LPMs FA values ipsilateral to the deviation side between T0 and T1, which may be related to improved muscle cross sectional areas and volumes, in line with previous studies.¹⁵ Taking into account that FA measures the magnitude of water molecule diffusion in an anisotropic tissue, the greater value at T1 is likely to be associated with volume increase together with a greater diameter of LPM muscle fibers due to improved mandibular mobility.

However, this study is prone to several limitations. First of all, we evaluated only two patients with

mandibular asymmetry, therefore our results should be taken as a grain of salt and we encourage further study to support the post-surgery diffusivity changes detected in the presented study. Then, some technical inherent limitations of DTI and tractography have to be taken into account. It is well known that DWI is potentially prone to motion artefacts at the data acquisition stage. In order to mitigate this issue, we used a single-shot, diffusion weighted EPI sequence along with sensitivity encoding. Second, low SNR may lead to erroneous estimation of diffusivity parameters (*i.e.* FA), therefore we decided to set the number of diffusion directions to 32 and to perform a denoising approach during the pre-processing step. In addition, in order to be sure that fiber orientation and FA estimation were not affected by inter-scans motions, we registered the diffusion-weighted images to the non-weighted image (B0) using an affine transformation and subsequently transformed the b-value matrix. Another limitation in DTI is using voxels with large sizes (in the present study $2 \times 2 \times 2$ mm³); indeed, if on the one hand using larger voxels increase the SNR, on the other hand, this become challenging in areas more susceptible to partial volume effects. Finally, it should be noted that DTI and tractography are not able to measure sarcomere length (which is approximately in the range of 2–3 µm).

In conclusion, despite the above-mentioned intrinsic-DTI limitations, our preliminary data suggest that the LPM of the side ipsilateral to the crossbite shows a clear impairment along with a significant improvement after BSSO of the mandible.

These preliminary findings suggest the potential use of diffusion MRI and tractography for the study of muscular stomatognathic dysfunction. However, further studies with mandibular asymmetry patients, and a larger sample size, should be fostered to fully evaluate effectiveness of BSSO on LPMs, to improve our knowledge on the potential of DTI in the evaluation of TMJD and to realize more accurate pre-surgical plans.

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