Tinnitus and musculoskeletal parameters: correlations between range of motion, muscle stiffness and tinnitus related disability in patients with and without chronic pain:
A cross sectional observational study

A Master's dissertation

Joris Van Oijen (01704309), Simon Van de Velde (01704390)

Promotor: Dr. Kayleigh De Meulemeester
Copromotor: Dra. Dorine Lenoir

A dissertation submitted to Ghent University in partial fulfilment of the requirements for the degree of Master in Rehabilitation Sciences and Physiotherapy.

Academic year: 2021 - 2022

GHENT UNIVERSITY

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Contents

LIST OF TABLES AND FIGURES

LIST OF ABBREVIATIONS

Abbreviation	Definition
CSI	Central sensitization questionnaire
HQ	Hyperacusis Questionnaire
ICC	Intraclass Correlation Coefficient
MAS	M. Masseter
MSM	Mean Shear Modulus
MSS	Musculoskeletal
NRS	Numeric Rating Scale
ROI	Region Of Interest
ROM	Range Of Motion
SCM	M. Sternocleidomastoideus
SD	Standard Deviation
SPC	M. Splenius Capitis
SWE	Shear Wave Elastography
TFI	Tinnitus Functional Index
THI	Tinnitus Handicap Inventory
TI	Tinnitus Impact
TMJ	Temporomandibular Joint
TRD	Tinnitus Related Disability
TRP	M. Trapezius
TSCHQ	Tinnitus Sample Case History Questionnaire

ABSTRACT (ENGLISH)

Background: Tinnitus is a common symptom located in the auditory system and it is defined as the perception of a phantom sound that affects up to 30% of the human population at any time. Tinnitus can be divided into objective and subjective tinnitus and can lead to a plethora of accompanying problems, cumulating in a heterogeneous pool of symptoms referred to as tinnitus related disability (TRD). Subjective tinnitus can be linked to somatosensory input and this can modulate the function of several musculoskeletal (MSS) structures. Current research has mostly looked at clinical evaluations of MSS parameters. Objective measurement strategies can be of added value for understanding the link between the two afferent information streams. Furthermore, since tinnitus is often accompanied by chronic pain, its influence on these relationships should be investigated more thoroughly.

Aim: The aim of this experimental study is to determine: (1) the potential correlations between TRD and neck/ temporomandibular joint (TMJ) range of motion (ROM), (2) between TRD and muscle stiffness and (3) to determine if there are any differences when analyzing these potential correlations in a tinnitus population with and without chronic pain.

Study design: cross sectional observational study

Methods: A cross sectional observational study was performed on 42 participants. Tinnitus functional index (TFI) and tinnitus impact (TI) were assessed as depictions for TRD. ROM of the neck and TMJ were measured with the EasyAngle and muscle stiffness was measured via shear wave elastography (SWE). The presence of chronic pain was acquired by means of a baseline questionnaire. Spearman correlation and regression analyses were performed for the overall population and per group. To calculate the power of this study a post hoc power analysis was performed.

Results: A significant correlation between TMJ opening ROM and both TFI and TI was found. Regression analyses revealed that the variance of the TRD, measured by TFI and TI score, could be explained by TMJ opening ROM for 16,4% and 14,9% respectively. A significant correlation was found between the mean shear modulus (MSM) of the left trapezius muscle in participants without chronic pain and TFI score, no significant linear regression was found. Post hoc power analysis revealed a high change of type II error for all outcome measures.

Conclusion: The results show no significant correlations between TRD and cervical ROM or muscle stiffness. Only a significant correlation was found between TRD and TMJ opening ROM. No difference was found between participants with and without chronic pain. Because of the low post hoc analysis power scores this dissertation should be interpreted as an explorative/pilot study. Future research

should focus on reassuring the quality of the study by: (1) using a larger sample size; (2) utilizing more valid, reliable and standardized TI, ROM and muscle stiffness measurement strategies; (3) adding a group of healthy control participants and (4) adapting of the inclusion criteria in order to achieve a less heterogenic population focused on somatic tinnitus patients.

ABSTRACT (NEDERLANDS)

Achtergrond: Tinnitus is een veelvoorkomend symptoom dat zich in het auditieve systeem bevindt en wordt gedefinieerd als de perceptie van een fantoomgeluid dat tot 30% van de menselijke bevolking treft. Tinnitus kan worden onderverdeeld in objectieve en subjectieve tinnitus en kan leiden tot een overvloed aan begeleidende problemen, dit cumuleert in een heterogene poel van symptomen ook wel tinnitus-gerelateerde invaliditeit (TRD) genoemd. Subjectieve tinnitus kan worden gekoppeld aan somatosensorische input en dit kan de functie van verschillende musculoskeletale (MSS) structuren moduleren. In het huidige onderzoek is vooral gekeken naar klinische evaluaties van MSS-parameters. Objectieve meetstrategieën kunnen een meerwaarde zijn om het verband tussen de twee afferente informatiestromen te begrijpen. Bovendien, aangezien tinnitus vaak gepaard gaat met chronische pijn, zou de invloed hiervan op deze relaties grondiger moeten worden onderzocht.

Doel: De doelstelling van deze experimentele studie is om: (a) de potentiële correlaties tussen TRD en spierstijfheid en (b) tussen TRD en het bewegingsbereik (ROM) van de nek en het kaakgewricht (TMJ) te onderzoeken en (c) te bestuderen of er verschillen zijn in deze potentiële correlaties wanneer er geanalyseerd wordt voor deelnemers met chronische pijn en deelnemers zonder chronische pijn.

Studie design: cross sectionele observationele studie

Methodes: Een cross sectionele observationele studie werd uitgevoerd met 42 deelnemers. De Tinnitus functional index (TFI) en tinnitus impact (TI) zijn verzameld als uitdrukkingen van TRD. ROM van de nek en TMJ zijn gemeten met de EasyAngle en de spierstijfheid is gemeten met shear wave elastografie (SWE). De aanwezigheid van chronische pijn is bevraagd via de baseline vragenlijst. **Spearman c**orrelaties en regressies zijn geanalyseerd voor de volledige populatie en per groep. Om de power van deze studie te berekenen is er een post hoc power analyse uitgeoverd.

Resultaten: Een significante correlatie tussen de ROM van het kaakgewricht en zowel de TFI en de TI werd gevonden. Uit regressieanalyses bleek dat de variantie van de TRD, gemeten met TFI en TI-score, kon worden verklaard door TMJ-openings-ROM voor respectievelijk 16,4% en 14,9%. Een significante correlatie werd gevonden tussen de mean shear modulus (MSM) van de linker trapezius spier en de TFI en deelnemers zonder chronische pijn, hiervoor werd geen significante lineaire regressie gevonden. De post hoc power analyse liet een grote kans op type II fouten zien.

Conclusie: De resultaten laten geen significante correlaties zien tussen TRD en cervicale ROM of spierstijfheid. De enige significante correlatie die gevonden werd was tussen TRD en TMJ-openings-ROM. Er werd geen verschil gevonden voor deelnemers met en zonder chronische pijn. Vanwege de zwakke post hoc power scores moet dit document geïnterpreteerd worden als een verkennende/pilot studie. Toekomstig onderzoek moet focussen op het verzekeren van kwaliteit door: (1) het gebruik van meer deelnemers; (2) het gebruik van valide, betrouwbare en gestandaardiseerde meetstrategieën voor TI, ROM en spierstijfheid; (3) het toevoegen van een groep van gezonde controleparticipanten en (4) aanpassen van de inclusiecriteria om een minder heterogene populatie, gefocust op somatosensorische tinnitus, te bekomen.

Trefwoorden: chronische tinnitus, minder validiteit, spierstijfheid, bewegingsbereik, chronische pijn

INTRODUCTION

Tinnitus is a continuous perception of a phantom sound in the absence of a corresponding external acoustic stimulus and is a common symptom located in the auditory or neurological system (1–3), affecting up to 30% of the human population (4). Higher prevalence can be observed among the elderly and male population (5–9). In addition, smoking, sleep deprivation, hyperlipidemia, excessive noise exposure, stress and depression are considered prevailing risk factors (10–13). These perceptions can have a large variety in their tinnitus characteristics: type of sound, loudness, pitch, intensity, continuity and frequency (14,15). It is advised to take these tinnitus characteristics into consideration since associations can be found with tinnitus related disability (TRD) (15). TRD, also called tinnitus-related handicap, can be defined as the disability which accompanies the tinnitus in daily living (15). TRD can be measured with several questionnaires, e.g. Tinnitus functional index (TFI), Tinnitus handicap inventory (THI), Visual analogue scale scores etc.. Several studies show the importance and heterogeneity of TRD, reporting that tinnitus can have an association with feelings of depression, distress, anxiety, insomnia and a decrease in Quality of Life (16–19). The complexity of TRD is accentuated by potential bothersome associated disorders, such as hyperacusis, temporomandibular joint and/or cervical spine disorders alongside coexisting symptoms like pain in the ear, nausea, dizziness and headaches etc (20–24).

Tinnitus is generally classified into two types: objective tinnitus and subjective tinnitus (25,26). Objective tinnitus is the only type of tinnitus which can be heard by an external observer and is frequently synchronous with the heartbeat (26). Subjective tinnitus, however, is the most common (e.g.: 99% of all tinnitus patients in the U.S.A. (27)) and exhibits a wide variety in intensity and absolute duration of the symptoms (26,28). This study will focus on participants with chronic subjective tinnitus, which is defined as 'subjective tinnitus lasting for a minimum duration of three months, for a minimum five minutes per day and is present on the majority of days in the week (≥ 4/7)' (29). Subjective tinnitus is regularly classified into two specific subtypes: sensory tinnitus and conductive, (26). Sensory tinnitus is associated with deterioration of the auditory system (26). Somatic or conductive tinnitus is linked to somatosensory input and research shows that the activity of several musculoskeletal (MSS) structures in the head, neck, temporomandibular joint (TMJ) and eyes can modulate this specific subtype of subjective tinnitus, this is called somatic modulation (28,30–32). On average, somatic modulation of tinnitus characteristics is seen in 69% of all tinnitus patients (33,34). It is documented that tinnitus

patients have more physical complaints in the TMJ and neck than people without tinnitus (35–39). Although this subclassification in subjective tinnitus is accepted and used in the tinnitus literature, there are some doubts about whether or not this classification is clinically useful. These concerns are proposed in a study regarding the subclassification of subjective tinnitus (40).

A possible explanation for the link between somatic modulation and tinnitus characteristics is that there is a connection between the cervical somatosensory- and the auditory system (41–43). They both send sensory input via afferent nerve fibres to the auditory cortex, which means that auditory impulses can be altered by somatosensory input originating from any structure projecting to the cervical somatosensory system (41–44). Tinnitus can therefore be influenced by (dys)function of the neck and/or jaw (31–34), e.g. articular dysfunction and/or muscle stiffness (45).

Tinnitus and pain show many similarities. Both are subjective sensations with a possibility to turn chronic. Both are often accompanied by hypersensitivity in their respective sensory system and overlapping brain changes have been observed (46). Because of the theoretical similarities between tinnitus and chronic pain, a potential positive correlation can be hypothesized between chronic pain and TRD. One study claimed that this relationship has never been investigated (46).

The potential influence of articular dysfunction and/or muscle stiffness on TRD has mostly been researched through clinical evaluations (47). To investigate this influence, objective and representative measurements are needed to evaluate these elements. Multiple methods can be applied for quantifying these parameters. A wide variety of questionnaires are available that attempt to objectify TRD: Tinnitus Questionnaire, Tinnitus Reaction Questionnaire, THI and TFI. For articular range of motion (ROM) several methods can be used, such as radiography, gonio/inclinometers, and electromagnetic tracking devices (48). Muscle stiffness can be measured, among others, via manual palpation, myotomometry and elastography.

A paucity of research exists about the correlation between TRD on one hand and cervical and TMJ articular ROM or muscle stiffness on the other. These correlations in the overall tinnitus population and the tinnitus population with and without chronic pain need further research. Due to the theoretical connections between these elements, a possible correlation can be expected.

The purpose of this study was to investigate if there is a correlation between TRD and MSS parameters in patients suffering from subjective tinnitus and whether or not this relationship is different in tinnitus patients with and without chronic pain.

In order to answer this research question, three objectives were postulated: (1) To investigate a possible correlation between TRD and cervical spine and TMJ ROM. (2) To investigate a possible

correlation between TRD and cervical and facial muscle stiffness. (3) To examine the possible differences between the hypothetical aforementioned correlations when analyzing the group with and without chronic pain. In this study, it is hypothesized that there will be a negative correlation between tinnitus and articular range of motion; there will be a positive correlation between tinnitus and muscle stiffness and there will be a stronger correlation between TRD and both ROM and muscle stiffness for the tinnitus group with chronic pain.

METHODS

1 Study design

This cross-sectional, observational study was approved by the Committee for Medical Ethics of Ghent University/UZ-Gent (code: BC-07036). The questionnaires were filled in individually at home by the participants and all data were collected at Ghent University hospital. Participants signed an informed consent form before the start of the physiotherapeutic assessment.

2 Population

2.1 Sample size calculation

A convenience sample was used for this cross sectional observational study.

2.2 Recruitment

Participants were recruited by using different media which include the distribution of a flyer (see Appendix 1), e-mail, hand-delivery in ear-nose-throat clinical centres of hospitals, general practitioners' practices, a wide variety of different companies, factories and public places in and around Ghent and via online sharing of the flyer on Facebook 'tinnitus support groups' and other Facebook groups. Recruitment started at the end of August 2021 and was finished in mid-March 2022.

2.3 Inclusion and exclusion criteria

Once potential participants signed up via e-mail, they were asked to fill in an inclusion questionnaire, which is included in appendix 2, in order to check the participant's eligibility. Participants were included if they met **all** the inclusion criteria: patients with chronic subjective tinnitus, aged between 18 and 65 years, and able to speak and understand Dutch fluently were included. For a detailed depiction of the in- and exclusion criteria, see table 1.

Inclusion criteria	Exclusion criteria
Aged between 18-65 years	Objective tinnitus
Speaking and understanding Dutch fluently	Pulsatile tinnitus
Chronic subjective tinnitus (> 3 months during most of the days/week and for more than 5 minutes/day)	Subjective tinnitus caused by clear causes such as tumour, trauma, vascular dysfunction, neurological disorders
	Vertigo (Menière's disease, Benign paroxysmal positional vertigo,…)
	Deafness
	Subjects with prior otologic surgery (for example stapedotomy), active outer or middle ear pathology
	Wearing a hearing aid device, implant, noise generators or receiving neuromodulation therapy
	Intracranial pathologies
	History of head, neck or shoulder trauma or surgery
	Major depression or psychiatric illness (diagnosed by a psychiatrist and being in medical or psychiatric treatment)
	Life-threatening, metabolic, cardiovascular, neurologic, systemic diseases
	Diagnosis of fibromyalgia/chronic fatigue syndrome
	Pregnancy or given birth in the preceding year
	Taking muscle relaxants or medication that has an influence on muscle tension and cognition
	Dyslexia, dyscalculia, AD(H)D, language/communication disorder

Table 1: In- and exclusion criteria.

3   Data collection

Three outcome measures were evaluated for this study, being: TRD, ROM and muscle stiffness. Each participant filled in a baseline questionnaire (see Appendix 2) in order to rate their TRD and underwent a physiotherapeutic assessment session to objectify their cervical/mandibular ROM and muscle stiffness.

3.1   Tinnitus related disability

TRD data was acquired via two questionnaires, being: TFI and TI. The TFI and TI scores are the main outcome measures that were used for the analysis of the results.

3.1.1   Tinnitus Functional Index

Participants were asked to fill in the TFI to quantify their subjective tinnitus complaints. This is a self-report questionnaire that contains 25 questions which the participant scores on a scale from zero to ten and the total score can range from zero to 100 points (49). Higher scores reflect greater tinnitus severity and a more negative impact on the participants everyday life. The total TFI score registers the following grades of tinnitus severity: no problem (0–17 points); small problem (18–31 points);

moderate problem (32– 53 points); big problem (54–72 points); and a very big problem (73–100 points) (49). This questionnaire was developed by Meikle et al (49) and it has been shown to be valid and reliable for treatment-related change, comprehensive coverage of the domains of tinnitus impact and other psychometric properties (in the cognitive, sleep, relaxation, quality of life and emotional subscales) (50,51). It covers a wide range of domains within the International Classification of Functioning, Disability and Health (42). Thus, the TFI score can be interpreted as a representative depiction of subjective tinnitus complaints and TRD. The TFI questionnaire was sent to the participants via e-mail and was filled in by the participants at home, participants could e-mail the researchers if they had questions or problems while filling in the TFI.

3.1.2 Tinnitus Impact

Tinnitus impact (TI) was acquired via the baseline questionnaire. Participants were asked to rate the impact of their tinnitus on their daily functioning on a scale from zero to ten, with zero being 'no impact at all' and ten being 'maximal impact'. This questionnaire is composed as a numeric rating scale (NRS).

3.2   Range of motion

The EasyAngle device was employed for the ROM measurement. It is a digital goniometer which can calculate the inclination of a segment relative to a tester-determined starting position in degrees. One study showed that the EasyAngle is as valid as another validated goniometer in a healthy population for cervical rotation (53).

The range of motion of flexion, extension, bilateral rotation and bilateral lateral flexion of the full cervical spine; bilateral upper cervical spine rotation (the cervical flexion-rotation test) and maximal opening of the mandible were measured. Table 2 describes the positioning of the participant and the EasyAngle during ROM measurements. Appendix 3 reveals photos of the measurements with the EasyAngle.

Movement	Positioning of the participant	Positioning of the EasyAngle
Flexion of the full cervical spine	Seated in a chair with the feet hip-width apart, hands resting on their thighs and cervical spine in a neutral position	Ventro-cranially to the right ear in the sagittal plane
Extension of the full cervical spine		
Rotation of the full cervical spine (bilateral)		Cranially in respect to the ear contralateral to the movement in the transverse plane
Lateral flexion of the full cervical spine (bilateral)		Ventro-cranially to the ear contralateral to the movement in the frontal plane
Rotation of the upper cervical spine (the flexion-rotation test, bilateral)	Supine position with a pad under the knees, arms pronated and relaxed on the table next to the body with the cervical spine in full flexion	Cranially in respect to the ear contralateral to the movement in the transverse plane
Opening of the mandible	Seated in a chair with the feet hip-width apart, hands resting on their thighs and cervical spine in a neutral position	Against the body of the mandible in the sagittal plane

Table 2: Description of the performed movements for ROM analysis, positions in which they were tested and the position of the EasyAngle relative to the plane in which the movement took place.

Every movement was repeated three times and after every repetition the participant was requested to return to the starting position, equalling zero degrees on the EasyAngle. The participant was instructed to perform the movements solely in the cervical spine/ TMJ and avoid compensation in the shoulders and thoracic regions, repeating measurements that showed compensation. The end of the movement was determined when moderate resistance or pain was reported by the participant. All tests were aborted in the presence of signs of dizziness and/or nausea.

3.3 Muscle stiffness

3.3.1 Measurement strategy

Muscle stiffness was measured using shear wave elastography (SWE) (Aixplorer Supersonic Imagine SSI Aixplore – MACH30). The SWE transducer produces an acoustic radiofrequency force impulse, generating a transversely oriented shear wave. This provides data on the inherent elasticity of tissue and biomechanical information about tissue quality (54). SWE has been validated for measurement along the main axis of the muscle, irrespective of fibre pennation for the M. Biceps brachi for healthy controls (55). Another study found moderate to good reliability of the SWE measurement for the M. Masseter (MAS), M. Sterno- cleidomastoideus (SCM), M. Splenius capitis (SPC), M. Trapezius pars descendens (TRP) and the M. Semispinalis capitis in healthy controls (56).

Four different muscles were analysed bilaterally in this study: MAS, SCM, SPC and TRP. The locations for measurement of these muscles were marked with a dermographic pencil. Table 3 shows a detailed description of the anatomical landmarks.

Table 3: Description of the position in which the SWE was measured and the exact location of the anatomical landmarks of the four measured muscles in SWE analysis.

Muscle	Position	Location
M. Masseter	Lying in supine position with a pad under the knees and the arms relaxed on the table in pronation next to the body.	The masseter muscle in the widest part (the midpoint level) of the muscle in the belly. The middle part of the masseter muscle was identified while the participant clenched his/her teeth on the most protruding part of the muscle (57).
M. Sternocleidomastoideus		An anatomical landmark was placed halfway between the sternoclavicular joint and the mastoid process, in the middle of the muscle belly (58)
M. Splenius Capitis	Lying in prone position + with a pad under the ankles. The arms lying relaxed on the table at their sides and the forehead resting in the notch of the table.	Two centimetres lateral to the spinous process of the fourth cervical vertebra (59).
M. Trapezius pars descendens		Two centimetres lateral of the midway between the lateral edge of the acromion and the spinous process of the seventh cervical vertebra (59).

In order to perform the measurement, the shear wave transducer L18/5 was lubricated with Aquasonic® ultrasound gel to improve the quality of the images and positioned on the landmarks. The probe was aligned with the shortening direction of the target muscle fibres. The following settings were employed: SWE unit in 'kPa', optimization on 'penetration', Opacity on '100%', Range on '100 kPa', Persistence turned 'off', Smoothing on '5', display format on 'side by side', Dynamic range on '65 decibels', Gain on '90%', image depth on '0-3 centimetre' and brightness on '90-100%'. Probe pressure was minimized by employing solely gravity (without applying additional pressure) and the same position of the probe was ensured for each trial. The individuals were instructed to relax, breathe slowly, remain silent and not to cough, swallow or sneeze during the measurements. For every muscle, three recordings of five seconds were captured, releasing the probe in-between measurements. If necessary, an initial slight adjustment of the perpendicular transducer angle was enabled to improve

the image. One recording captured 96 frames. Of every recording, seven frames were analysed using Matlab.

3.3.2 Matlab analysis

Matlab R2021b was used for the analysis of the SWE footage. First, the DICOM files made with the SWE machine were uploaded to a shared server. From this, files were exported to ElastoGUI where the Region Of Interest (ROI) was drawn manually. To avoid fascia, bone, hypoechoic regions and areas without stiffness values; the region of interest included especially muscle fibres. To ensure this, an irregular shape was manually drawn avoiding all tissue that was not of interest, an example of this can be found in Appendix 4. To analyse the images, saturation was set to 100 kPa. Within the ROI, ElastoGUI analyses the images for shear modulus, void, saturation and ROI area. All DICOM files were analysed per participant and exported into an excel file which was then imported into SPSS 27.

3.4 Chronic pain

Participants were divided into two groups: tinnitus with chronic pain and tinnitus without chronic pain. Participant's eligibility for this allocation was decided based on their answers formulated in the baseline questionnaire. The participants were classified into the chronic pain group if they met all inclusion criteria: pain for at least three months, a pain intensity of at least 3/10 in the month preceding the test moment, and pain for more than three days a week.

4 Statistical analysis

4.1 Descriptives, correlations and regression analyses

The data was organised and analysed via SPSS 27. First, the normality of the data was checked in order to know whether parametric or non-parametric tests should be performed. Second, Spearman correlations between TFI/TI and ROM/SWE were analysed. In the case of a significant correlation, linear regression analyses were used to determine the relationships between ROM, muscle stiffness and TFI/TI scores. A bivariate regression analysis was employed to determine the association between: (1) TFI/TI scores and ROM values and (2) TFI/TI scores and muscle stiffness. A p-value of ≤0.05 was considered to indicate a statistically significant association between the variables.

4.2 Post hoc power analyses

Post hoc power analyses were performed with G*Power 3.1.9.2[1] (60,61). A 'correlation: bivariate normal model statistical test' was performed for all non-significant correlations (62,63). An example of the use of G*Power can be found in Appendix 5.

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[1] G*Power is a data analytics software to compute statistical power analyses for many commonly used statistical tests in social and behavioral research. It can also be used to compute effect sizes and to graphically display the results of power analyses (104).

RESULTS

1. Descriptives

The data of 42 participants were analysed in this study. One value was absent for the following parameters: BMI, Tinnitus loudness (acquired via the tinnitus sample case history questionnaire (TSCHQ), TFI, Hyperacusis questionnaire (HQ) and Central Sensitization Inventory (CSI). Two values were absent for tinnitus frequency. A detailed description of all missing data can be found in the discussion (see Discussion: 3.: Missing data). A per-protocol analysis was used for the analysis of the missing data.

The baseline data of all the included participants are presented in Table 4.

	Data[1]	Range
Age (in years) (n=42)	41,14 (±14,96)	18-62
Gender (female/male) (n=42)	14/28 (33,33/66,67) ^	/
BMI (n=41)	24,71 (±3,51)	19,80-32,20
Tinnitus frequency (constant/intermittent) (n=40)	36/4 (85,70/14,30) ^	/
Tinnitus duration (in years) (n=42)	10,86 (±7,76)	2-35
TI (0-10) (n=42)	3,23 (±2,77)	0-10
Tinnitus loudness (via TSCHQ) (0-100) (n=41)	43,17 (±22,76)	3-85
TFI (0-100) (n=41)	24,26 (±19,95)	0,80-80,10
Hyperacusis (present/not present) (n=42)	25/17 (59,50/40,50) ^	/
HQ (0-42) (n=41)	18,83 (±8,52)	3-40
Chronic pain (present/not present) (n=42)	15/27 (35,70/64,30) ^	/
CSI (0-100) (n=41)	28,80 (±13,75)	5-60

Table 4: Descriptive statistics for the complete population. [1] Data are mean (±standard deviation (sd)) or the number of participants (percentage(%)) indicated via ^. The number of participants that data was available for is represented by 'n'.

The population was divided into two groups: participants with chronic pain and participants without chronic pain. Baseline data per group and a comparison of the means are presented in Table 5. A significant difference in the means of both groups was found for three variables: presence of hyperacusis, the HQ score and the CSI score. All three variables were significantly higher in the tinnitus group with chronic pain. All other variables showed no significant differences.

	Tinnitus without chronic pain[1] (n=27)	Tinnitus with chronic pain[1] (n=15)	Difference of the means[2] (p value)
Age (in years)	40,85 (±14,88)	41,67 (±15,62)	0,870
Gender (female/male)	9/18 (33,33/66,67)^	5/10 (33,33/66,67)^	1,000
BMI	23,94 (±2,93)	26,05 (±4,11)	0,094
Tinnitus frequency (constant/ intermittent)	23/4 (85,20/14,80)^	13/1 (86,67/6,67)^ [3]	0,658
Tinnitus duration (in years	9,53 (±5,81)	13,23 (±10,21)	0,212
TI (0-10)	2,57 (±2,16)	4,40 (±3,40)	0,074
Tinnitus loudness (via TSCHQ) (0-100)	41,74 (±22,94)	45,93 (±23,00) [3]	0,583
TFI (0-100)	20,07 (±18,69)	32,34 (±20,48) [3]	0,061
Hyperacusis (present/not present)	13/14 (48,10/51,90)^	12/3 (80/20)	0,044*
HQ (0-42)	16,33 (±7,44)	23,64 (±8,65) [3]	0,013*
CSI (0-100)	24,22 (±10,98)	37,64 (±14,58) [3]	0,006*

Table 5 : Comparison in descriptive statistics between the tinnitus groups with and without chronic pain. [1] Data are mean (±sd) or a number of participants (percentage(%)), number of participants is indicated via ^. [2] Difference of the means was calculated via the unpaired student's t-test for continuous variables and via the Chi-Square test for categorical variables. The number of participants that data was available for is represented by 'n'. [3] indicates one missing set of data for the given parameter, resulting in 14 full data sets.

Chronic-pain-specific descriptives are summarized in Table 6. Pain locations were cumulative, meaning that participants who had chronic pain in multiple locations are reported multiple times in Table 6. Neck, TMJ and head were of the main interest because nociceptive information for these structures could impact tinnitus parameters as described in the introduction.

Pain location	Amount of times this location is impacted by chronic pain	Average pain duration in years (missing data)	Average pain score in the last month (via NRS) (missing data)
Neck	17	5,74 (8)	3,65 (6)
TMJ	2	0,66 (1)	7,00
Head	6	12,5 (4)	3,60 (1)
Others*	27	9,00 (8)	3,63 (1)

*Table 6: pain-specific descriptives of participants with chronic pain. * Others: e.g. knee, elbow, lower back.*

2   Range of motion analysis

2.1   Descriptives

Descriptive statistics of the ROM for all the included participants are presented in Table 7. The descriptive statistics of both groups separately and a comparison of means are presented in Table 8. The two groups were not significantly different. Each participant was available for analysis except for the TMJ opening ROM for one participant, who was included in the tinnitus with chronic pain group. All ROM variables are normally distributed, statistical analysis of normality for ROM outcomes can be seen in Appendix 6.

	Mean (in degrees) (± SD)	Range (in degrees)
Flexion	60,47 (12,03)	32,3 – 84,3
Extension	64,10 (12,42)	40,7 – 89,7
Rotation Left	69,64 (11,13)	45,0 – 100,3
Rotation Right	73,21 (10,44)	48,7 – 91,7
Lateral flexion Left	39,70 (8,23)	25,3 – 53,7
Lateral flexion Right	38,12 (8,40)	23,0 – 57,0
Rotation of the upper cervical spine Left	53,19 (9,85)	23,0 – 70,7
Rotation of the upper cervical spine Right	52,86 (9,82)	30,7 – 72,0
Opening of the mandible	29,43 (5,72)	20,0 – 45,3

Table 7: Descriptives of ROM

	Mean (in degrees) (±SD)		Difference of the means[1] (p-value)
	Chronic pain	No chronic pain	
Flexion	58,29 (±8,49)	61,68 (±13,61)	0,327
Extension	61,62 (±14,06)	65,48 (±11,46)	0,341
Rotation Left	67,64 (±10,54)	70,75 (±11,49)	0,393
Rotation Right	70,60 (±10,88)	74,65 (±10,11)	0,233
Lateral flexion Left	41,72 (±6,93)	38,58 (±8,79)	0,241
Lateral flexion Right	37,91 (±9,08)	38,24 (±8,18)	0,906
Rotation of the upper cervical spine Left	53,55 (±13,74)	53,00 (±7,16)	0,886
Rotation of the upper cervical spine Right	53,26 (±11,29)	52,64 (±9,14)	0,848
Opening of the mandible	27,26 (±4,84)	30,55 (±5,90)	0,080

Table 8: descriptive statistics of ROM for both groups and comparison of the means. [1] Difference of the means was calculated via the unpaired student's t-test.

2.2   Correlation

Table 9 depicts the Spearman correlation grid for all participants. A non-significant correlation for flexion, extension, lateral flexion, rotation, and upper cervical spine rotation was found between these variables and TI or TFI score. Rotation of the upper cervical spine was excluded from analysis (see Discussion 3: Missing data).

TMJ opening ROM showed a significant correlation with both TFI (r=-0,315) and TI score (r=-0,416) indicating a weak, negative correlation between TMJ opening ROM and both TI and TFI score for the full population.

Tables 10 and 11 show the correlation grids after dividing the population respectively in tinnitus without and with chronic pain. Non-significant correlations were found for every movement when analysing both groups separately.

Correlations for all participants		Flexion	Extension	Lateral flexion left	Lateral flexion right	Rotation left	Rotation right	TMJ opening
TFI	R	0,01	-0,13	0,02	-0,15	-0,13	-0,22	-0,32*
	Sig. (2-tailed)	0,97	0,41	0,92	0,36	0,41	0,16	0,05
	N	41	41	41	41	41	41	40
Tinnitus impact	R	0,13	-0,11	-0,05	-0,04	-0,11	-0,26	-0,42**
	Sig. (2-tailed)	0,40	0,51	0,75	0,79	0,50	0,10	0,01
	N	42	42	42	42	42	42	41

Table 9: Correlations for all participants. R = correlation coefficient. **. Correlation is significant at the 0.01 level (2-tailed). *. Correlation is significant at the 0.05 level (2-tailed).

Correlations: Tinnitus without chronic pain		Flexion	Extension	Lateral flexion left	Lateral flexion right	Rotation left	Rotation right	TMJ opening
TFI	R	0,12	-0,30	-0,13	-0,13	-0,16	-0,12	-0,32
	Sig. (2-tailed)	0,56	0,13	0,52	0,52	0,42	0,54	0,11
	N	27	27	27	27	27	27	27
Tinnitus impact	R	0,28	-0,26	-0,30	-0,24	-0,15	-0,33	-0,38
	Sig. (2-tailed)	0,16	0,19	0,13	0,24	0,45	0,09	0,05***
	N	27	27	27	27	27	27	27

Table 10: Correlations for the group without chronic pain. R = correlation coefficient. *** indicates: the actual value was 0,051 which was not considered to be significant. **. Correlation is significant at the 0.01 level (2-tailed). *. Correlation is significant at the 0.05 level (2-tailed).

Correlations: Tinnitus with chronic pain			Flexion	Extension	Lateral flexion left	Lateral flexion right	Rotation left	Rotation right	TMJ opening
TFI	R		-0,24	0,24	0,12	-0,19	0,00	-0,34	-0,12
	Sig. (2-tailed)		0,42	0,40	0,69	0,52	0,99	0,23	0,69
	N		14	14	14	14	14	14	13
Tinnitus impact	R		0,05	0,26	0,32	0,26	0,09	0,01	-0,28
	Sig. (2-tailed)		0,86	0,36	0,24	0,35	0,74	0,96	0,33
	N		15	15	15	15	15	15	14

Table 11: Correlations for the group with chronic pain. R = correlation coefficient.
**. Correlation is significant at the 0.01 level (2-tailed). *. Correlation is significant at the 0.05 level (2-tailed).

2.3 Linear regression

2.3.1 Tinnitus impact and temporomandibular joint opening range of motion

Linear regression analysis reveals a significant linear regression ($R^2 = 0,149$) meaning that 14,9% of the variance of TI is caused by the TMJ opening ROM. Figure 1 depicts this approximated linear regression curve.
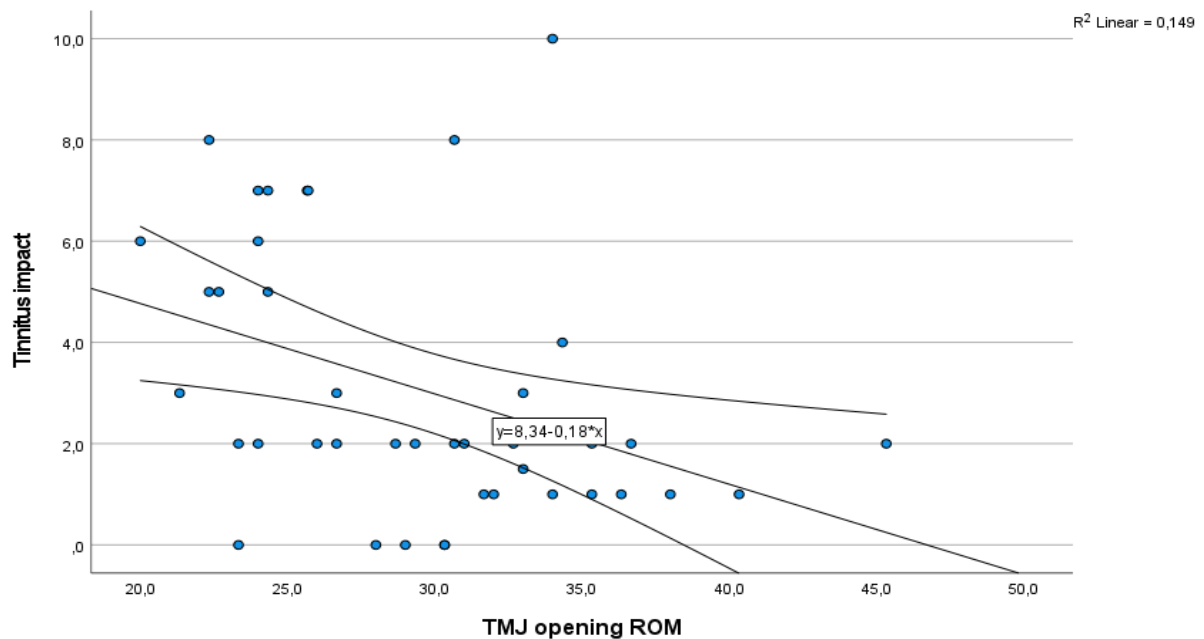
Figure 1: Linear regression curve for TI and TMJ opening ROM.

2.3.2 Tinnitus functional index and temporomandibular joint opening range of motion

Linear regression reveals a significant linear regression (R^2 = 0,164) meaning that 16,4% of the variance of the TFI score is caused by the TMJ opening ROM. Figure 2 depicts this approximated linear regression curve.
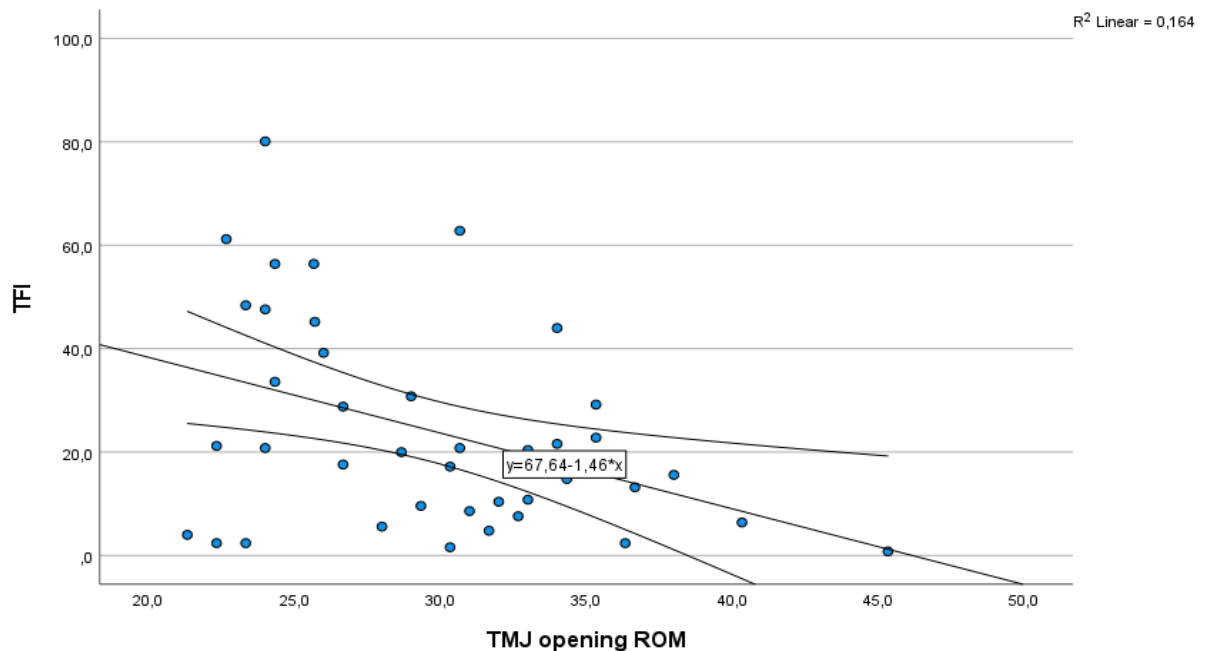
Figure 2: Linear regression curve for TFI and TMJ opening ROM.

2.3.3 Others

No other Spearman correlations were found, so no other regression models were analysed.

2.4 Post hoc power analyses

Post hoc power for ROM and TFI/TI was poor (64) for all movements and can be found in Appendix 13. The chance that a non-significant correlation occurred when a possible significant correlation should be found ranges from 61,12% to 94,96%, indicating a very high chance of a false-negative result. No power analyses were performed per group since the lower number of participants will most likely lead to an even worse power.

3 Shear wave elastography analysis

3.1 Descriptives

Four different parameters for muscle stifness were analysed during this study. The mean shear modulus (MSM), the void, the saturation and the ROI. The MSM was the main outcome of interest in this study as this is the most representative of the muscle stiffness. The other variables are indicative of the quality of the data. The void represents the area within the ROI that could not be analysed due to a lack of quality of the image. The saturation depicts how much the MSM value exceeds the maximal detectable value of the MSM in percentage. The ROI is the area within the Q-box of the SWE image that contains as much of the muscle of interest without fascia and other structures. Depending on the size of the muscle of interest, the ROI area will vary in size (e.g. Larger ROI for the TRP than for SPC). High quality of the data is thus indicated by a low value of the void and saturation. Descriptive statistics of the SWE for all the included participants are presented in Tables 13-16. Not all data was available for every participant, missing cases are represented in Table 12. A detailed description of all missing data can be found in the discussion (see Discussion: 3.: Missing data).

The descriptive statistics of both groups separately and a comparison of means are presented in Tables 17-20. Both the MSM of MAS and TRP were normally distributed. The MSM of the SCM and SPC were not normally distributed. Statistical analysis of normality for ROM outcomes can be seen in Appendix 14.

The MSM did not differ per group for any muscle except for the MSM of the right SCM which was significantly higher for the group without chronic pain, meaning that the average MSM of the right SCM of the group without chronic pain was 12,9 kPa higher than in the group with chronic pain. The mean of the ROI area of the right TRP differs per group with the chronic pain group having an average ROI area of 3,79 cm^2 larger when compared to the other group.

Muscle	Left				Right			
	MAS	SCM	SPC	TRP	MAS	SCM	SPC	TRP
Missing data	3	2	12	2	3	2	12	1

Table 12: Missing values for SWE data.

Masseter			
		Mean (±SD)	Range
Left (n=39)	Mean shear modulus	94,45 (±4,31)	40,40 – 161,58
	Void (%)	0,37 (±1,27)	0,00 – 7,79
	Saturation	16,70 (±2,50)	0,01 – 119,85
	ROI area	21,46 (±6,05)	9,67 – 32,93
Right (n=39)	Mean shear modulus	95,24 (±9,62)	0,00 – 8,57
	Void (%)	0,37 (±1,40)	0,01 – 100,51
	Saturation	14,66, (±22,02)	0,01 – 100,51
	ROI area	21,42 (±5,10)	9,26 – 32,11

Table 13: Descriptive statistics of the Masseter muscle.

Sternocleidomastoid			
		Mean (±SD)	Range
Left (n=40)	Mean shear modulus	70,54 (±1,93)	34,31 – 190,73
	Void (%)	1,82 (±4,92)	0,00 – 27,35
	Saturation	3,12 (±8,88)	0,00 – 40,21
	ROI area	18,47 (±6,14)	7,98 – 28,41
Right (n=40)	Mean shear modulus	66,25 (±1,94)	36,26 – 114,26
	Void (%)	7,89 (±14,76)	0,00 – 68,79
	Saturation	1,29 (±4,32)	0,00 – 22,12
	ROI area	17,92 (±5,21)	9,20 – 28,46

Table 14: Descriptive statistics of the Sternocleidomastoid muscle.

Splenius Capitis		Mean (±SD)	Range
Left (n=30)	Mean shear modulus	81,24 (±3,90)	34,81 – 181,55
	Void (%)	3,06 (±7,82)	0,00 – 36,52
	Saturation	9,87 (±18,71)	0,00 – 79,75
	ROI area	0,90 (±0,86)	0,42 – 4,13
Right (n=30)	Mean shear modulus	86,27 (±4,19)	53,21 – 155,80
	Void (%)	4,75 (±9,16)	0,00 – 36,53
	Saturation	13,82 (±20,95)	0,00 – 68,30
	ROI area	1,25 (±1,28)	0,47 – 4,18

Table 15: Descriptive statistics of the Splenius Capitis muscle.

Trapezius		Mean (±SD)	Range
Left	Mean shear modulus (n=40)	98,89 (±3,41)	43,48 – 199,80
	Void (%) (n=41)	0,09 (±0,23)	0,00 – 0,94
	Saturation (n=40)	8,14 (±18,56)	0,00 – 88,80
	ROI area (n=40)	20,40 (±6,11)	8,74 – 32,42
Right (n=41)	Mean shear modulus	87,39 (±3,27)	44,39 – 172,66
	Void (%)	0,25 (±1,46)	0,00 – 9,36
	Saturation	2,64 (±5,44)	0,00 – 27,19
	ROI area	20,66 (±5,50)	8,83 – 32,81

Table 16: Descriptive statistics of the Trapezius muscle.

Masseter					
	Mean (± SD)		Difference of the means (*p*-value)	Mean (± SD)		Difference of the means (*p*-value)
Side	Left			Right		
Group	Chronic pain (n=14)	No chronic pain (n=25)		Chronic pain (n=14)	No chronic pain (n=25)	
Mean shear modulus	93,50 (±2,12)	94,98 (±4,94)	0,879	84,28 (±4,58)	101,37 (±8,87)	0,116
Void (%)	0,31 (±0,53)	0,40 (±1,55)	0,826	0,07 (±0,16)	0,55 (±1,73)	0,315
Saturation	18,45 (±22,45)	15,73 (±26,08)	0,744	8,89 (±11,71)	17,90 (±25,74)	0,225
ROI area	21,84 (±6,79)	21,24 (±5,72)	0,769	21,25 (±4,88)	21,53 (±5,32)	0,871

*Table 17: Descriptive statistics of the SWE variables of the Masseter muscle for both groups and comparison of the means. * indicates a significant difference when comparing both groups.*

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Sternocleidomastoid						
	Mean (± SD)		Difference of the means (*p*-value)	Mean (± SD)		Difference of the means (*p*-value)
Side	Left			Right		
Group	Chronic pain (n=14)	No chronic pain (n=26)		Chronic pain (n=14)	No chronic pain (n=26)	
Void (%)	3,27 (±7,15)	1,05 (±3,06)	0,177	9,81 (±12,24)	6,86 (±16,09)	0,554
Saturation	3,31 (±9,90)	3,02 (±8,49)	0,923	0,01 (±0,01)	1,99 (±5,26)	0,066
Mean shear modulus	64,34 (±1,57)	73,88 (±1,76)	0,301	57,86 (±1,77)	70,77 (±2,02)	0,038*
ROI area	18,23 (±6,28)	18,60 (±6,19)	0,857	16,82 (±5,13)	18,50 (±5,26)	0,338

*Table 18: Descriptive statistics of the SWE variables of the M. Sternocleidomastoid for both groups and comparison of the means. * indicates a significant difference when comparing both groups.*

Splenius Capitis					
	Mean (± SD)		Difference of the means (*p*-value)	Mean (± SD)		Difference of the means (*p*-value)
Side	Left			Right		
Group	Chronic pain (n=11)	No chronic pain (n=19)		Chronic pain (n=10)	No chronic pain (n=20)	
Mean shear modulus	83,65 (±3,79)	79,85 (± 3,96)	0,759	84,91 (± 4,40)	86,95 (± 4,08)	0,840
Void (%)	1,78 (± 3,95)	3,80 (± 9,40)	0,506	5,34 (±9,47)	4,46 (±9,24)	0,810
Saturation	10,80 (±19,87)	9,34 (± 18,55)	0,841	19,90 (± 23,41)	10,78 (± 19,52)	0,269
ROI area	0,68 (± 0,14)	1,02 (± 1,06)	0,188	1,38 (±1,41)	1,19 (± 1,24)	0,966

*Table 19: Descriptive statistics of the SWE variables of the Splenius Capitis muscle for both groups and comparison of the means. * indicates a significant difference when comparing both groups.*

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Trapezius						
	Mean (± SD)		Difference of the means (*p*-value)	Mean (± SD)		Difference of the means (*p*-value)
Side	Left			Right		
Group	Chronic pain (n=15)	No chronic pain		Chronic pain (n=15)	No chronic pain (n=26)	
Mean shear modulus	103,72 (± 3,56)	96,00 (±3,32) (n=25)	0,475	85,20 (± 3,59)	88,65 (± 3,81)	0,709
Void (%)	0,08 (± 0,24)	0,08 (±0,23) (n=26)	0,954	0,03 (± 0,04)	0,37 (± 1,83)	0,478
Saturation	9,68 (±23,53)	7,22 (± 15,32) (n=25)	0,690	3,68 (± 7,86)	2,04 (± 3,41)	0,357
ROI area	21,52 (±7,14)	19,73 (± 5,44) (n=25)	0,375	23,06 (± 5,57)	19,27 (± 5,06)	0,032*

*Table 20: Descriptive statistics of the SWE variables of the Trapezius muscle for both groups and comparison of the means. * indicates a significant difference when comparing both groups.*

3.2 Correlations

Table 21 depicts the Spearman correlation between MSM values per muscle and TI and TFI score. No significant correlation could be found for all variables when analysing all participants. Tables 22 and 23 show the Spearman correlation grids after dividing the population respectively in tinnitus without and with chronic pain. Non-significant correlations were found between every MSM and both TI and TFI score when analysing both groups separately, apart from the TFI score and the MSM of the left TRP in the group without chronic pain (r=0,416). This indicates a weak positive correlation between muscle stiffness in the left TRP and TFI score in the group without chronic pain.

Correlations for all participants									
		Left				Right			
		MAS	SCM	SPC	TRP	MAS	SCM	SPC	TRP
TFI	r	0,02	-0,17	0,06	0,23	0,10	-0,14	-0,00	0,11
	Sig. (2-tailed)	0,92	0,30	0,77	0,17	0,57	0,39	0,99	0,52
	N	38	39	30	39	38	39	30	40
TI	r	-0,16	-0,07	-0,24	-0,01	0,00	-0,20	-0,19	0,06
	Sig. (2-tailed)	0,34	0,69	0,21	0,54	1,0	0,21	0,31	0,72
	N	39	40	30	40	39	40	30	41

*Table 21: Spearman correlations between MSM values per muscle and the TFI score and TI for all participants. * indicates a significant difference when comparing both groups.*

Correlations: Tinnitus without chronic pain									
		Left				Right			
		MAS	SCM	SPC	TRP	MAS	SCM	SPC	TRP
TFI	r	0,05	-0,26	-0,21	0,42	0,17	-0,04	-0,03	0,18
	Sig. (2-tailed)	0,83	0,20	0,93	0,04*	0,42	0,83	0,89	0,38
	N	25	26	19	25	25	26	20	26
TI	r	0,02	-0,24	-0,20	-0,04	0,23	-0,14	-0,28	0,14
	Sig. (2-tailed)	0,93	0,25	0,41	0,85	0,26	0,49	0,23	0,48
	N	25	26	19	25	25	26	20	26

Table 22: Spearman correlations between MSM values per muscle and the TFI score and TI for the group with chronic pain. * indicates a significant difference when comparing both groups.

Correlations: Tinnitus with chronic pain									
		Left				Right			
		MAS	SCM	SPC	TRP	MAS	SCM	SPC	TRP
TFI	r	0,08	0,14	0,22	-0,20	0,26	0,02	0,32	-0,00
	Sig. (2-tailed)	0,80	0,66	0,52	0,48	0,38	0,96	0,37	0,99
	N	13	13	11	14	13	13	10	14
TI	r	-0,40	0,23	-0,28	-0,27	-0,16	-0,21	-0,01	-0,08
	Sig. (2-tailed)	0,16	0,44	0,40	0,32	0,58	0,48	0,97	0,79
	N	14	14	11	15	14	14	10	15

Table 23: Spearman correlations between MSM values per muscle and the TFI score and TI for the group with chronic pain. * indicates a significant difference when comparing both groups.

3.3   Regression

Linear regression analysis reveals a non-significant linear regression (p=0,367) meaning that no linear model could be fitted for the correlation between the TFI score and the MSM of the left TRP in participants without chronic pain.

3.4   Post hoc power analyses

Post hoc power for SWE and TFI/TI was poor (64) for all muscles and can be found in Appendix 19. The chance that a non-significant correlation occurred when a possible significant correlation should be found ranges from 71,61% to 95,00% indicating a very high chance of a false-negative result. No power analyses were performed per group since the lower number of participants will most likely lead to an even worse power.

DISCUSSION

1.   Discussion of our hypotheses

The aim of this study was (1) to investigate a possible correlation between TRD and both cervical spine and TMJ ROM, (2) to investigate a possible correlation between TRD and both neck and fascial muscle stiffness and, (3) to examine the possible differences between the hypothetical aforementioned correlations when analyzing the tinnitus group with and without chronic pain. In order to properly examine these relations, three hypotheses were postulated before the start of the analysis:

a. There will be a negative correlation between TRD and articular ROM

b. There will be a positive correlation between TRD and muscle stiffness

c. There will be a stronger correlation between TRD and both ROM and muscle stiffness for the tinnitus group with chronic pain than in the tinnitus group without chronic pain.

These hypotheses were proposed based on the connection between the cervical somatosensory- and the auditory system (41–45,65–73). Assuming that tinnitus negatively influences the somatosensory system and/or vice versa, we would expect less articular ROM and higher muscle stiffness in participants with higher amounts of TRD. Progressing on this rationale, participants of whom the tinnitus is accompanied by chronic pain would show an even larger effect of TRD on the MSS parameters and/or vice versa.

2   Synthesis of our results

2.1   Tinnitus related disability and range of motion

2.1.1   Tinnitus related disability and temporomandibular joint opening range of motion

The linear regression coefficient entails that a portion of the variance of the TI, 14,9%, and the TFI score, 16,4%, is caused by the TMJ opening ROM. These findings are supported by a recent systematic review and meta-analysis on the association between tinnitus and TMJ disorders (74). This study concluded that signs of TMJ disorders may augment the likelihood of developing tinnitus, and the perception of tinnitus may also promote the signs of TMJ disorders. Another study found a significant correlation between tinnitus, measured via the THI, and TMJ disorders in participants suffering from both tinnitus and TMJ disorders (75). A review about the development and validity of tools for the measurement of tinnitus to assess handicap and treatment effects (76), demonstrated acceptable-to-high convergent validity between the total scores of the THI and TFI (77). A significant moderate correlation (p <0,001, r= 0,562) and a regression coefficient (p <0,001, R^2= 0,391) were found in this study between the TFI score and TI score, indicating that both measurement strategies for TRD are interrelated, for statistical analyses of this correlation and regression coefficient see Appendix 20-23. This suggests that the conclusion of this study may be generalized according to the results of current

literature. Another study found a causal role of TMJ disorders in the generation and maintenance of tinnitus (78,79). Based on the results of this study and the convincing evidence of previous research, screening for TMJ disorder symptoms in participants with tinnitus and suggesting an appropriate treatment of TMJ disorders (47,74) with current clinical approaches might lead to a reduction in tinnitus perception. This is especially the case for participants with limited TMJ ROM.

2.1.2 Tinnitus related disability and cervical range of motion

No significant correlation was found between TRD and ROM of the neck. An explanation for this result can be that the population did not solely consist of participants with somatosensory tinnitus and the overall small sample sizes used in this study. A two-sided relationship between somatosensory tinnitus subtype and TMJ, head and neck movement has been suggested in a recent study (80). A recent systematic review and meta-analysis supports this theory, showing evidence for a unidirectional correlation between subjective tinnitus and cervical spine disorders (81). This would suggest that participants with tinnitus report cervical spine disorders more frequently. Although an association was found, this was based upon the analysis of four studies that could not be included in the meta-analysis due to the lack of data of the controls. The included studies have some methodological limitations[2]. Nonetheless, the association is shown in participants that did not specifically suffer from somatosensory, but rather from subjective tinnitus making the population more comparable to the population of this study. Based on this, it can be concluded that there is a need for high-quality research into the association between general subjective tinnitus and cervical spine disorders in order to form a better understanding of this relationship.

2.2 Tinnitus related disability and muscle stiffness

A significant correlation was found between TRD and the MSM of the left TRP in the tinnitus group without chronic pain (r= 0,416) but no linear regression model could be fitted for this relationship. This means that there is a weak to moderate positive relationship between TRD and the muscle stiffness of the left TRP in tinnitus participants that do not suffer from chronic pain. This relationship is positively non-linear meaning that with an increase in TRD, the muscle stiffness increases but this is not proportional to the increase in TRD. When comparing this to the correlations of the left and right TRP of the other populations, the coefficients do not come close to a significant result insinuating that the significance might be a coincidence. No studies have reported this specific finding in the literature. One

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[2] Shortcomings: no random selection of cases and controls; no matching of the controls to the cases; no clearly defined, valid, reliable and implemented exposure to measures across all participants ; and no information about the blinding of the assessors about the case or control condition of the participants. At least two of these limitations were present in all of the included studies.

study on normative data of SWE values in healthy controls has reported a higher muscle tension in the left (non-dominant) TRP than in the right (dominant) TRP, but the difference was not significant (82).

No further significant correlations were found between TRD and muscle stiffness. This could as well be explained by the fact that the population of this study did not solely consist of participants with somatosensory tinnitus and the overall small sample sizes used in this study. No studies supporting these results could be found, the following rationale is purely based on a hypothesis provided by the authors. A well-researched treatment strategy for somatosensory tinnitus is manually reducing muscle tension and deactivating myofascial trigger points in the neck and jaw muscles (80,83). From this, it may be concluded that there must be a relationship between muscle tension and tinnitus. Unfortunately, since SWE is a relatively recent technology and this is the first study to investigate the association between tinnitus and muscle stiffness measured via SWE meaning that no comparative research was available. A study on cervicogenic headache reports significantly higher muscle tension in the SCM in participants suffering from cervicogenic headache than in controls, tinnitus and SCM muscle tension might interact in a similar pattern (84). Comparing the results with reference values of healthy subjects for the muscles analysed in this research project, a difference seems apparent from the current results, see Appendix 24 (82). Remarkable is the much higher value for the MAS in this study while all other MSM values are similar or lower than the normative data. This could be explained by the causal relationship between TMJ disorders and tinnitus described by another study (85). This could mean that, although only one correlation was found between TRD and muscle stiffness, a higher tension in the masseter muscle may also be present in participants with tinnitus than in healthy controls. Caution should be taken when interpreting these results. Firstly, the normative data are based on a dataset of ten healthy volunteers. Such a small sample size limits the generalizability, which would improve with the addition of a control group. Secondly, no statistical analyses were done to compare the different results. Lastly, all normative data were based on right-handed subjects. In this study the majority were right-handed (n=38), but four subjects were left-handed.

Comparing these results to the postulated hypotheses, it can be concluded that the findings of this study tend to align with the pre-proposed hypothesis that there would be a weak positive correlation between TRD and muscle stiffness since one significant correlation was found. Although this finding could be coincidental. Nonetheless, based on the comparison between the normative data and the data of this study, it may be assumed that participants suffering from tinnitus can experience higher muscle tension in the left TRP and right MAS muscle than healthy controls. An explanation for this may be the possible presence of somatosensory tinnitus within the population of this study. Note that this conclusion should be interpreted with caution due to the fact that there is no statistical evidence supporting these results. Nonetheless, the values seem promising.

2.3 Tinnitus related disability and chronic pain

The current study included a group with tinnitus and chronic pain and a group with tinnitus but without chronic pain. No analysis was performed on the relation between tinnitus and chronic pain. When inspecting the literature, an association between these elements can be assumed (69,86,87). Consensus among these studies largely exists about both conditions having a similar pathophysiology, further suggesting a relationship between the two (69,88). However, current knowledge of this relationship is largely based upon small clinical studies (73) or studies of specific pain syndromes (89–91) which limits the generalisability of these results.

Based on the findings of this study, chronic pain does not seem to affect the association between TRD and MSS parameters, since no significant correlations were found. An explanation for this result can be that the population did not solely consist of participants with somatosensory tinnitus and the overall small sample sizes used in this study. Although current literature suggests a relationship, no correlations were found in this or other studies. This result differs from the postulated hypothesis: no correlation was found but suggested a weaker correlation for the chronic pain group.

3 Missing data

Although the amount of missing data and information is quite limited, some are noteworthy while interpreting the results: SWE missing data, an uncompleted baseline questionnaire and a case of missing data in the ROM measurements.

Due to a change in strategy[3], SWE images were analysed via ElastoGUI. For this reason, the first SWE datasets were captured with a brightness setting that was too low for analysis via ElastoGUI, rendering them unusable for further statistical analysis. This led to several images of participants being categorized as missing data. Brightness settings must be higher than 90% for ElastoGUI to analyze the imported images, which was not necessary for manual analysis. Images captured with a low brightness setting were not analysed manually to keep methodological consistency. A summary of the missing data in the SWE can be found in Appendix 25. Furthermore, SPC images were often difficult to capture due to the pronounced cervical lordosis and SWE imaging could not be performed on the MAS with bearded participants (n=1).

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[3] Initially it was planned to analyse all data manually, after a couple weeks of testing (pre-analysis) it was decided to analyse the SWE data via ElastoGUI. A software program which would lead to a time-saving and a more methodological strict way of analyzing the SWE images.

One participant did not fill in the baseline questionnaire. This led to an absence of the tinnitus loudness, TFI, CSI and HQ score. This participant was excluded from all analyses in relation to the TFI.

The data of the TMJ opening ROM measurement of one participant was lost during the course of the study. No analysis regarding the TMJ opening ROM correlations was performed for this participant.

Another methodological shortcoming was the indistinct answers of participants to the questions regarding the baseline data. The depicted average duration of pain and tinnitus were often described vaguely. In order to collect the data consistently two rules were applied: (1) if participants gave a range of time[4] or (2) when participants answered 'at least …'[5], the minimum value was used. One participant was categorized in the tinnitus without chronic pain group but indicated to have a chronic pain location that has not caused him/her pain for the past 6 months with a sporadic flare-up.

Rotation of the upper cervical spine was excluded from analysis due to an incongruence with normative data. Average upper cervical rotation in this study was $53,19° \pm 9,85°$ and $52,86° \pm 9,82°$ for respectively left and right upper cervical rotation, no normative data was found for tinnitus participants. Normative data of the upper cervical rotation measurements in healthy controls are 44 degrees on average for both left and right upper cervical rotation (92). This indicates that our measurements were probably biased due to a measurement fault.

4   Strengths and weaknesses

This experimental study is the first one using SWE and EasyAngle for the evaluation of MSS-parameters in a tinnitus population. This innovation brings forth a gateway for further research as well as methodological shortcomings.

Four main weaknesses should be considered when interpreting this study. First, the lack of literature containing reliability and validation of the EasyAngle. Second, methodological difficulties in SWE analysis. Third, the use of TI as a scoring device. Fourth, poor post hoc power analysis scores.

The EasyAngle was employed to measure the ROM. In a German study, the EasyAngle is shown to be as reliable as the Cervical Range Of Motion Instrument, another validated inclinometer (44), for rotation of the cervical spine in healthy individuals (45). There is no other evidence that shows that the EasyAngle is validated for every direction measured in this study nor is there evidence showing reliability in participants with neck and/or jaw disorders. This limits the generality of the findings in this study.

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[4] E.g. 10-20 years
[5] E.g. 'at least 10 years'

Because of the lack of supporting literature for the reliability of the EasyAngle, a small inter- and intra-tester reliability study was performed. See Appendices 26-32 for methods, results, statistical analysis and conclusions of this study.

Inter-rater reliability showed excellent reliability in four movements: flexion, extension, lateral flexion right and upper cervical rotation left. Good reliability was found in three movements: lateral flexion left, rotation left and upper cervical rotation right. Two movements showed moderate reliability: rotation right and TMJ opening. The average intraclass correlation coefficient (ICC) of all movements is 0,848 meaning that the average ICC of the EasyAngle shows good reliability for the movements performed in this study.

Intra-rater reliability showed excellent reliability in seven movements: flexion, extension, lateral flexion left and right, rotation left and upper cervical rotation left and right. Good reliability was found in rotation right and moderate reliability was found in TMJ opening. The average ICC of all movements is 0,906 meaning that the average ICC of the EasyAngle shows excellent reliability for the movements performed in this study.

Four details to take into account when interpreting the conclusions deserve an additive amount of attention: (1) Due to the small sample size and the limited amount of statistical tests which were performed, the results of this study give an interesting indication but are not performed in a way that makes the lack of literature neglectable. (2) The intra-rater reliability is the most important ICC to analyse for interpreting the results of this dissertation because all testing in the tinnitus study was performed by one tester (KDM). (3) Intra-rater correlation showed to be excellent on average, making the results of the tinnitus study more trustworthy. (4) The one intra-rater reliability ICC which showed moderate reliability was the TMJ opening ROM (ICC= 0,747). Coincidental or not, this is the only movement in which a significant correlation between the TRD and ROM was found. A less reliable measuring device potentially influences this correlation.

Two types of methodological difficulties presented themselves regarding the analysis via ElastoGUI. First, every imported image of the muscles should have 96 frames. Seven frames were taken at regular time intervals during the recording and were analysed as a representative sample. Due to still unknown reasons, not all 96 frames of some images were imported into ElastoGUI, resulting in a different number of frames analysed for some muscles. Second, another difficulty unknown to the authors was the absence of analysis of some of the frames per image. The dataset exported from ElastoGUI showed most of the frames analysed correctly in combination with a couple of randomly blank exported

frames. Although not every image was analysed with the same number of frames, researchers made sure that every muscle had a sufficient amount of frames for a representative sample.

TI was composed like a NRS scale, although NRS scales have been shown to be reliable in all types of domains such as tinnitus annoyance and loudness (51,93,94), pain (95), psoriasis (96), dyspnea (97) as well as others (98,99); No literature supporting the validity and reliability of the NRS for TI could be found. This limits the generality of the findings in this study.

Poor post hoc power analysis scores show a high likelihood of the appearance of false-negatives in the results of this study. This indicates that all non-significant results are not as reliable as presented. Although the usefulness of post hoc power analyses is often criticized in current literature (100,101), the poor power scores indicate that this study should be interpreted as more of an explorative/pilot study and it would be highly beneficial to repeat the study with larger sample sizes. Using a larger sample size will improve the sensitivity of the study, lowering the change of a type II error and will lead to more reliable and trustworthy results (102).

Emphasizing the innovative nature of this study, four main strengths can be considered while interpreting the results. First, no other research has evaluated the relationship between TRD and MSS parameters via these objective strategies. The authors hope that this opens a new gateway in the field of tinnitus research. Second, before all data were collected, the full strategy for analysis of the data was finalized which was not adapted after data collection. This led to a methodological correct approach to documenting the results. Third, all tests were performed by one researcher (KDM), meaning that all collected data were gathered in a consistent and methodologically correct manner. Finally, due to the strict guidance and regular feedback of the promotors, this study was checked thoroughly.

5   Clinical implications

Screening for TMJ disorder in participants with tinnitus and suggesting an appropriate treatment with current clinical approaches might lead to a reduction in tinnitus perception. Especially for participants with limited TMJ ROM (47,74,79,85).

There does not seem to be a correlation between TRD and both cervical ROM and muscle stiffness, although participants suffering from tinnitus seem to have higher tension in the left TRP in participants without chronic pain than in participants with chronic pain and in the right MAS compared to healthy controls. Treatment via manually reducing muscle tension and deactivating myofascial trigger points might lead to a relief of TRD (80,82,83,85).

6   Recommendations for future research

There is a need for high-quality research into the association between general subjective tinnitus and cervical spine disorders in order to form a better understanding of the relationship between TRD and cervical ROM. More research is needed into the relationship between chronic pain and tinnitus and its influence on MSS parameters. The association between muscle stiffness, measured via SWE, and tinnitus should be inspected more thoroughly as well.

Due to the innovative nature of this study, multiple methodological shortcomings have been identified. Future research should focus on reassuring the quality of the study by (1) using a larger sample size, (2) utilizing more valid, reliable and standardized TI, ROM and muscle stiffness measurement strategies and (3) the addition of a group of healthy control participants. Furthermore, (4) adaptation of the inclusion criteria to achieve a less heterogenic population focussed on somatic tinnitus patients. This can be accomplished by assessing the influence of MSS parameters on subjective tinnitus perceptions in these subjects via questions like: "does your tinnitus seem to be influenced by movements of the neck, head or jaw?" included in the eligibility questionnaire. More research is needed for normative data of MSM measured by SWE and the validity and standardization of SWE analysis.

Interesting examples of analyses in future research may be the potential correlations between:

1. ROM and/or SWE and the location of the pain.
2. TFI score and/or TI score and the location of the pain.
3. Different pain locations in patients with and without chronic pain.
4. The side of the pain and the side of tinnitus.
5. TMJ opening ROM and MAS tension measured via SWE and its effect on TRD.
6. Chronic pain and TRD in somatic tinnitus patients.

GENERAL CONCLUSION

The results show no significant correlations between TRD and cervical ROM or muscle stiffness. Both a significant correlation and regression were found between TRD and TMJ opening ROM. No difference was found between participants with and without chronic pain. Because of the low post hoc analysis power scores this dissertation should be interpreted as an explorative/pilot study. Future research should focus on reassuring the quality of the study by: (1) using a larger sample size; (2) utilizing more valid, reliable and standardized TI, ROM and muscle stiffness measurement strategies; (3) adding a group of healthy control participants and (4) adapting the inclusion criteria in order to achieve a less heterogenic population focussed on somatic tinnitus patients.

APPENDIX

Appendix 1: Flyer which was used for recruiting the participants

Appendix 2: Inclusion and baseline questionnaire

In case of interest regarding the inclusion and/or baseline questionnaires, please contact kayleigh.demeulemester@ugent.be.

Appendix 3: Photos of the ROM measurement with the EasyAngle.

Flexion   Extension

Lateral Flexion left

Rotation left

Upper cervical rotation left

TMJ opening
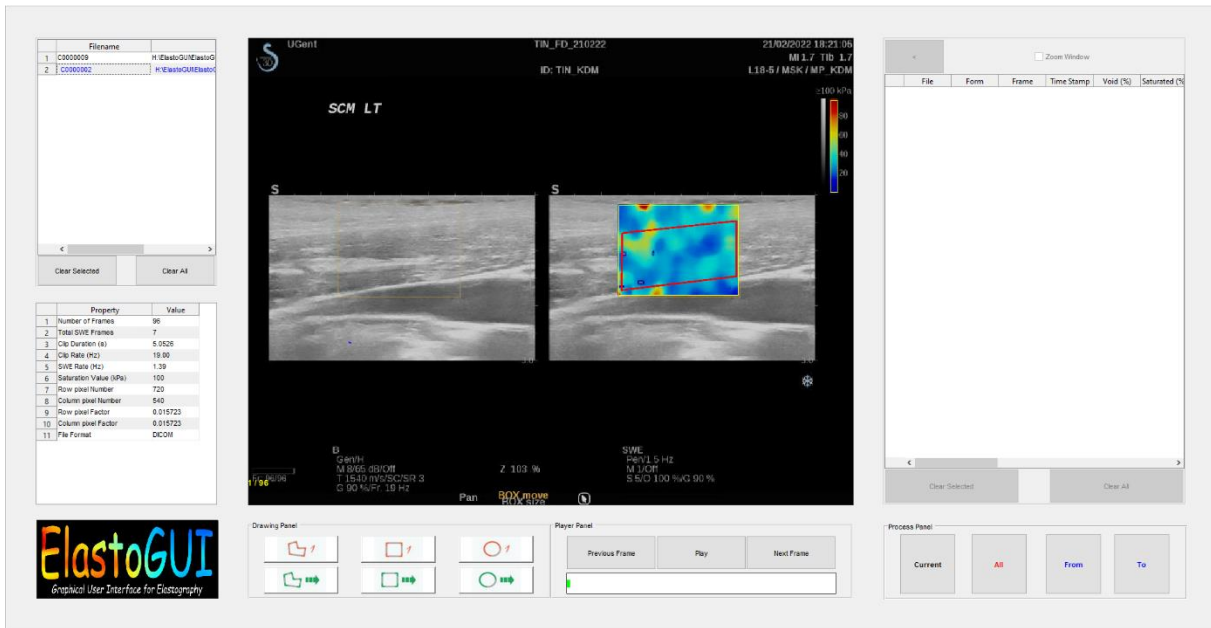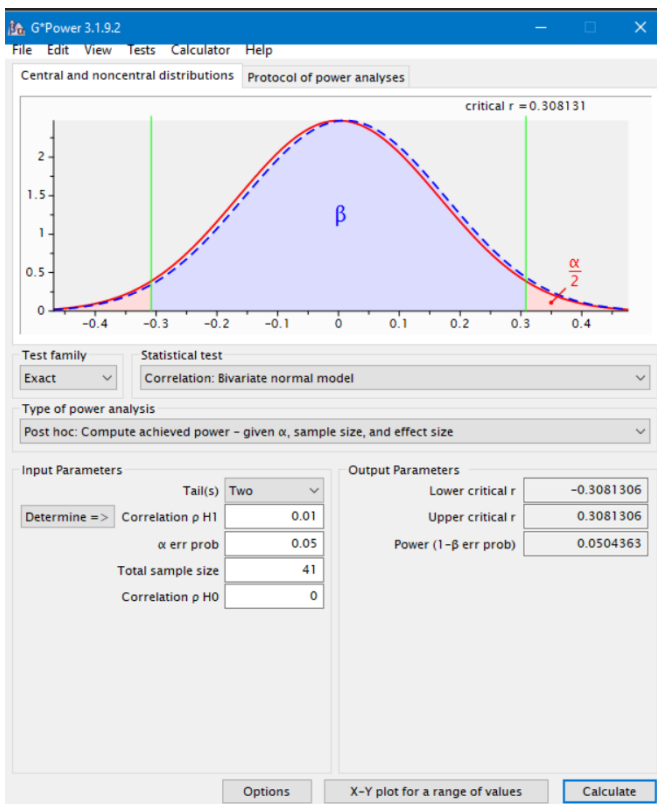
Appendix 6:Test of normality for ROM outcomes

Tests of Normality ROM						
	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Flexion	0,062	42	0,200[*]	0,992	42	0,988
Extension	0,102	42	0,200[*]	0,980	42	0,659
Lateral flexion left	0,095	42	0,200[*]	0,960	42	0,148
Lateral flexion right	0,112	42	0,200[*]	0,973	42	0,425
Rotation left	0,086	42	0,200[*]	0,981	42	0,717
Rotation right	0,094	42	0,200[*]	0,963	42	0,192
Upper cervical rotation left	0,139	42	0,039	0,950	42	0,063
Upper cervical rotation right	0,081	42	0,200[*]	0,981	42	0,704
TMJ opening	0,106	41	0,200[*]	0,965	41	0,230

*: This is a lower bound of the true significance. A: Lilliefors Significance Correction

Appendix 7: Model summary of regression analysis for TI and TMJ opening ROM.

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	0,385[a]	0,149	0,127	2,4767

a: Predictors: (Constant), TMJ opening ROM

Appendix 8:ANOVA analysis of regression analysis for TI and TMJ opening ROM.

	ANOVAᵃ				
Model	Sum of Squares	df	Mean Square	F	Sig.
1 Regression	41,723	1	41,723	6,802	0,013ᵇ
Residual	239,228	39	6,134		
Total	280,951	40			

a: Dependent Variable: TI. b: Predictors: (Constant), TMJ opening ROM

Appendix 9: Regression coefficients for TI and TMJ opening ROM

	Coefficientsᵃ						
	Unstandardized Coefficients		Standardized Coefficients			95,0% Confidence Interval for B	
Model	B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound
1 (Constant)	8,340	2,051		4,065	<0,001	4,190	12,489
TMJ opening ROM	-0,179	0,068	-0,385	-2,608	0,013	-0,317	-0,040

a: Dependent Variable: TI

Appendix 10: Model summary of regression analysis for TFI and TMJ opening ROM.

	Model Summary			
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	0,405ᵃ	0,164	0,142	18,7048

a: Predictors: (Constant), TMJ opening ROM

Appendix 11: ANOVA analysis of regression analysis for TFI and TMJ opening ROM.

ANOVA[a]						
Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	2613,890	1	2613,890	7,471	0,009[b]
	Residual	13294,980	38	349,868		
	Total	15908,870	39			

a: Dependent Variable: TFI

Appendix 12: Regression-coefficients for TFI and TMJ opening ROM.

Coefficients[a]								
		Unstandardized Coefficients		Standardized Coefficients			95,0% Confidence Interval for B	
Model		B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound
1	(Constant)	67,639	16,173		4,182	<0,001	34,898	100,381
	TMJ opening ROM	-1,465	0,536	-0,405	-2,733	0,009	-2,550	-0,380

a: Dependent Variable: TFI

Appendix 13: Post hoc power scores for ROM and TFI/TI.

	Flexion	Extension	Lateral flexion left	Lateral flexion right	Rotation left	Rotation right
TFI	0,0504	0,1277	0,0517	0,1549	0,1277	0,2846
TI	0,1298	0,1064	0,0613	0,0572	0,1064	0,3888

Appendix 14: Test of Normality for MSM.

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
Tests of Normality	Statistic	df	Sig.	Statistic	df	Sig.
MSM MAS left	0,116	37	0,200[*]	0,973	37	0,498
MSM MAS right	0,126	37	0,147	0,952	37	0,111
MSM SCM left	0,154	38	0,023	0,805	38	<0,001
MSM SCM right	0,195	38	<0,001	0,883	38	<0,001
MSM SPC left	0,154	28	0,086	0,903	28	0,014
MSM SPC right	0,142	28	0,155	0,917	28	0,029
MSM TRP left	0,064	38	0,200[*]	0,970	38	0,405
MSM TRP right	0,084	39	0,200[*]	0,964	39	0,248

*. This is a lower bound of the true significance.

Appendix 15: Model summary of regression analysis for TFI and MSM of the left TRP per group.

Model Summary[b]					
Group	Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
Tinnitus and no pain	1	0,184[a]	0,034	-0,006	18,9452
Tinnitus and pain	1	0,067[a]	0,004	-0,078	21,2669

a: Dependent Variable: TI. b: Predictors: (Constant), TMJ opening ROM

Appendix 16: ANOVA analysis of regression analysis for TFI and MSM of the left TRP per group.

Group	Model		Sum of Squares	df	Mean Square	F	Sig.
ANOVAª							
Tinnitus and no pain	1	Regression	303,012	1	303,012	0,844	0,367[b]
		Residual	8614,073	24	358,920		
		Total	8917,085	25			
Tinnitus and pain	1	Regression	24,357	1	24,357	0,054	0,820[b]
		Residual	5427,378	12	452,281		
		Total	5451,734	13			

a: Dependent Variable: TFI . b: Predictors: (Constant), MSM of left TRP

Appendix 17: Regression coefficients for TFI and MSM of the left TRP per group.

Group	Model		Unstandardized Coefficients B	Std. Error	Standardized Coefficients Beta	t	Sig.
Coefficientsª							
Tinnitus and no pain	1	(Constant)	10,567	11,479		0,921	0,366
		MSM right TRP	0,113	0,123	0,184	0,919	0,367
Tinnitus and pain	1	(Constant)	27,386	22,103		1,239	0,239
		MSM right TRP	0,058	0,250	0,067	0,232	0,820

a: Dependent Variable: TFI

Normal P-P plot of regression standardized residual of the TFI score and the MSM of the left TRP per group.

Normal P-P Plot of Regression Standardized Residual
Dependent Variable: TFI (/100)
Groep: Tinnitus and no pain

Normal P-P Plot of Regression Standardized Residual
Dependent Variable: TFI (/100)
Groep: Tinnitus and pain
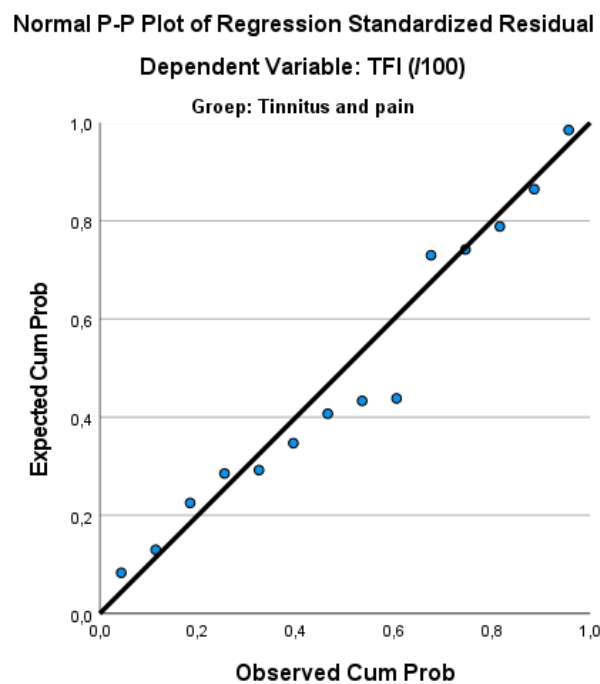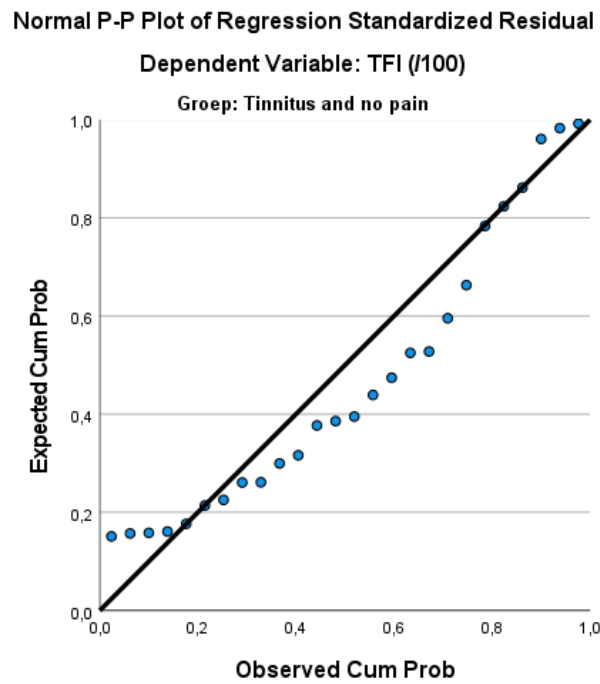
Appendix 19: Post hoc power scores for SWE and TFI/TI.

	Left				Right			
	MAS	SCM	SPC	TRP	MAS	SCM	SPC	TRP
TFI	0,0516	0,1791	0,0612	0,2939	0,0915	0,1358	0,0500	0,1034
TI	0,1636	0,0711	0,2503	0,0504	0,0500	0,2371	0,1717	0,0659

Appendix 20: Spearman correlation comparing TFI and TI

			TFI
Spearman's rho	Tinnitus impact	R	0,562[**]
		Sig. (2-tailed)	<0,001
		N	41

**: Correlation is significant at the 0.01 level (2-tailed)

Appendix 21: Model summary of regression analysis for TFI and TI.

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	0,626[a]	0,391	0,376	2,1894

a: Predictors: (Constant), TFI

Appendix 22: ANOVA analysis of regression analysis for TFI and TI.

ANOVA[ants]					
Model	Sum of Squares	df	Mean Square	F	Sig.
1	Regression	120,272	1	120,272	25,090	<0,001[b]
	Residual	186,948	39	4,794		
	Total	307,220	40			

a: Dependent Variable: TI. b: Predictors: (Constant), TFI

Appendix 23: Regression-coefficients for TFI and TI.

Coefficients							
	Unstandardized Coefficients		Standardized Coefficients			95,0% Confidence Interval for B	
Model	B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound
1 (Constant)	1,050	0,542		1,936	0,060	-0,047	2,147
TFI	0,087	0,017	0,626	5,009	<0,001	0,052	0,122

Appendix 24: MSM comparison between normative data[1] and the results of this study[2]

	MAS MSM (±SD)	SCM MSM (± SD)	SPC MSM (± SD)	TRP MSM (± SD)
Data[1]	55,57 (±0,94)	96,69 (± 1,49)	75,79 (± 3,19)	108,09 (± 3,53)
Data[2]	94,85 (± 6,97)	68,40 (±1,94)	83,76 (±4,05)	93,07 (±3,34)

Appendix 25: Summarization of missing data in MSM of SWE-analysis.

	Left				Right			
Muscle	MAS	SCM	SPC	TRP	MAS	SCM	SPC	TRP
Missing data	3	2	12	2	3	2	12	1

Appendix 26: Methods of the reliability study of the EasyAngle

Recruitment/participants: Ten participants were included. In- and exclusion criteria can be found in the table below.

Inclusion criteria	Exclusion criteria
Aged between 18-65 years	Objective tinnitus
Speaking and understanding Dutch fluently	Pulsatile tinnitus
Chronic subjective tinnitus (> 3 months during most of the days/week and for more than 5 minutes/day) *	Subjective tinnitus caused by clear causes such as tumour, trauma, vascular dysfunction, neurological disorders
	Vertigo (Menière's disease, BPPV,…)
	Deafness
	Subjects with prior otologic surgery (for example stapedotomy), active outer or middle ear pathology
	Wearing a hearing aid device, implant, noise generators or receiving neuromodulation therapy
	Intracranial pathologies
	History of head, neck or shoulder trauma or surgery
	Major depression or psychiatric illness (diagnosed by a psychiatrist and being in medical or psychiatric treatment)
	Life-threatening, metabolic, cardiovascular, neurologic, systemic diseases
	Diagnosis of fibromyalgia/chronic fatigue syndrome
	Pregnancy or given birth in the preceding year
	Taking muscle relaxants or medication that has an influence on muscle tension and cognition
	Dyslexia, dyscalculia, AD(H)D, language/communication disorder
	Chronic and acute subjective tinnitus**

Testing: ROM testing with the EasyAngle was performed via the exact same protocol that was used in the tinnitus study (see methods: 3. Data collection: 3.2.1. ROM). This protocol was used in three steps and two testers, JVO and SVV, performed the measurements. Each participant (1) was tested once by both testers, (2) received a twenty-minute break and (3) was tested once more by one researcher (SVV).

Analysis: Mean ROM was used for every participant and every movement. Due to a last-minute cancellation two datasets were used. Nine of the participants were used for both the inter- and intra-rater reliability, two different participants were used as the tenth participants. ICC was calculated in SPSS 27 via a reliability analysis. Inter-rater reliability was analysed with a two-way random model and an absolute agreement type on a 95% confidence interval. Intra-rater reliability was analysed a two-way mixed model and an absolute agreement type on a 95% confidence interval. ICC average measures were used for conclusions.

Participants descriptives of the inter-/intra-rater reliability study.

1. Inter-rater reliability

	N	Mean (+-SD)	Range
Age	10	21,50 (+-1,18)	19,00 – 23,00
BMI		22,11 (+-1,68)	20,00 – 25,10
Gender (female)		5	/

2. Intra-rater reliability

	N	Mean (+-SD)	Range
Age	10	21,60 (+-1,17)	19,00 - 23,00
BMI		22,03 (+-1,70)	20,00 - 25,10
Gender (female)		5	/

Appendix 28: ROM descriptives of the inter-/intra-rater reliability.

1. Descriptives ROM testing 1 J.V.: inter-rater reliability.

	N	Mean (+-SD)	Range
Flexion	10	56,20 (+-16,24)	39,00 – 90,00
Extension		70,27 (+-18,29)	36,33 – 93,67
Lateral flexion left		42,70 (+-7,21)	30,00 – 50,67
Lateral flexion right		45,63 (+-6,77)	29,33 – 53,33
Rotation left		81,47 (+-13,22)	56,33 – 104,00
Rotation right		80,73 (+-9,48)	63,33 – 96,00
Upper cervical rotation left		73,50 (+-14,88)	52,67 – 98,67
Upper cervical rotation right		71,07 (+-12,31)	49,33 – 94,33
TMJ opening		26,57 (+-4,98)	18,33 – 34,67

2. Descriptives ROM testing 1 S.V: inter-rater reliability.

	N	Mean (+-SD)	Range
Flexion	10	57,77 (+-12,98)	39,67 – 77,33
Extension		73,50 (+- 14,43)	50,33 – 90,00
Lateral flexion left		41,70 (+-7,96)	26,67 – 51,67
Lateral flexion right		46,90 (+-6,80)	30,33 – 54,67
Rotation left		80,00 (+-11,07)	63,67 – 104,33
Rotation right		81,10 (+-6,80)	71,67 – 95,33
Upper cervical rotation left		69,37 (+- 12,16)	54,33 – 94,67
Upper cervical rotation right		70,43 (+-9,86)	59,00 – 88,33
TMJ opening		27,07 (+-5,22)	17,33 – 34,67

3. Descriptives ROM testing: intra-rater reliability

		N	Mean (+-SD)	Range
First testing	Flexion	10	58,20 (±12,43)	43,33 – 79,67
	Extension		71,53 (±16,17)	40,33 – 95,67
	Left lateral flexion		42,67 (±8,67)	26,00 – 53,67
	Right lateral flexion		45,03 (±6,48)	29,33 – 52,67
	Left rotation		78,57 (±11,22)	62,67 – 104,33
	Right rotation		81,80 (±7,88)	67,00 – 95,33
	Left upper cervical rotation		71,40 (±11,94)	54,33 – 94,67
	Right upper cervical rotation		71,37 (±11,42)	51,33 – 88,33
	TMJ opening		27,77 (± 3,84)	21,00 – 34,67
Second testing	Flexion		58,14 (±15,06)	42,33 – 90,00
	Extension		70,20 (±18,46)	40,00 – 98,67
	Left lateral flexion		44,07 (±11,07)	28,00 – 67,33
	Right lateral flexion		43,90 (±5,83)	29,33 – 52,33
	Left rotation		79,77 (±11,32)	62,33 – 104,00
	Right rotation		79,57 (±7,15)	65,67 – 88,67
	Left upper cervical rotation		73,87 (±11,71)	57,33 – 98,67
	Right upper cervical rotation		71,83 (±11,63)	50,67 – 94,33
	TMJ opening		28,87 (±2,91)	25,00 – 34,67

		Intraclass Cor	Lower Bound	Upper Bound	Value	df1	df2	Sig
Inter-Rater Reliability: Interclass Correlation Coefficient			95% Confidence interval		F Test with True Value 0			
Flexion	Single Measures	0,862[a]	0,550	0,964	12,772	9	9	<0,001
	Average Measures	0,926	0,710	0,982	12,772	9	9	<0,001
Extension	Single Measures	0,891[a]	0,638	0,971	18,829	9	9	<0,001
	Average Measures	0,942	0,779	0,985	18,829	9	9	<0,001
Lateral Flexion Left	Single Measures	0,751[a]	0,272	0,932	6,614	9	9	0,005
	Average Measures	0,857	0,427	0,965	6,614	9	9	0,005
Lateral Flexion Right	Single Measures	0,839[a]	0,504	0,957	11,547	9	9	0,001
	Average Measures	0,913	0,671	0,978	11,547	9	9	0,001
Rotation Left	Single Measures	0,801[a]	0,388	0,946	8,505	9	9	0,002
	Average Measures	0,889	0,559	0,972	8,505	9	9	0,002
Rotation Right	Single Measures	0,442[a]	-0,282	0,829	2,427	9	9	0,101
	Average Measures	0,613	-0,784	0,907	2,427	9	9	0,101
Upper Cervical Rotation Left	Single Measures	0,824[a]	0,442	0,953	12,353	9	9	<0,001

	Average Measures	0,904	0,613	0,976	12,353	9	9	<0,001
Upper Cervical Rotation Right	Single Measures	0,758[a]	0,270	0,934	6,681	9	9	0,005
	Average Measures	0,862	0,426	0,966	6,681	9	9	0,005
TMJ opening	Single Measures	0,577[a]	-0,074	0,877	3,486	9	9	0,038
	Average Measures	0,732	-0,159	0,935	3,486	9	9	0,038

A two-way random-effects model where both people effects and measures effects are random. a: The estimator is the same, whether the interaction effect is present or not. b: Type A intraclass correlation coefficients using an absolute agreement definition.

Appendix 30: Results: Intra-rater reliability: ICC

		Intra-rater reliability: ICC.						
			95% Confidence Interval		F Test with True Value 0			
		Intraclass Cor	Lower Bound	Upper Bound	Value	df1	df2	Sig
Flexion	Single Measures	0,849[a]	0,493	0,960	11,086	9	9	0,001
	Average Measures	0,918[c]	0,661	0,980	11,086	9	9	0,001
Extension	Single Measures	0,915[a]	0,702	0,978	20,950	9	9	<0,001
	Average Measures	0,955[c]	0,825	0,989	20,950	9	9	<0,001
Left lateral flexion	Single Measures	0,841[a]	0,500	0,958	11,158	9	9	0,001
	Average Measures	0,914[c]	0,666	0,978	11,158	9	9	0,001
Right lateral flexion	Single Measures	0,850[a]	0,532	0,960	12,490	9	9	<0,001
	Average Measures	0,919[c]	0,694	0,980	12,490	9	9	<0,001
Left rotation	Single Measures	0,854[a]	0,526	0,961	11,935	9	9	0,001
	Average Measures	0,921[c]	0,689	0,980	11,935	9	9	0,001
Right rotation	Single Measures	0,768[a]	0,341	0,936	8,298	9	9	0,002
	Average Measures	0,869[c]	0,508	0,967	8,298	9	9	0,002
Left upper cervical rotation	Single Measures	0,926[a]	0,704	0,982	32,685	9	9	<0,001
	Average Measures	0,962[c]	0,827	0,991	32,685	9	9	<0,001

Right upper cervical rotation	Single Measures	0,897[a]	0,640	0,973	16,843	9	9	<0,001
	Average Measures	0,946[c]	0,780	0,987	16,843	9	9	<0,001
TMJ opening	Single Measures	0,596[a]	0,032	0,879	4,039	9	9	0,025
	Average Measures	0,747[c]	0,062	0,936	4,039	9	9	0,025

A two-way relation mixed-effects model where people effects are random and measures effects are fixed. a: The estimator is the same, whether the interaction effect is present or not. b: Type A intraclass correlation coefficients using an absolute agreement definition. c: This estimate is computed assuming the interaction effect is absent, because it is not estimable otherwise.

Appendix 31: Conclusions: inter-rater reliability.

Inter-rater reliability showed excellent reliability in four movements (flexion, extension, lateral flexion right and upper cervical rotation left) with an ICC higher than 0,9, good reliability was found in three movements (lateral flexion left, rotation left and upper cervical rotation right) (ICC ranging between 0,75 and 0,9) and two movements showed moderate reliability (rotation right and TMJ opening) (ICC ranging between 0,5 and 0,75)(103). Each ICC score showed to be significant. The average ICC of all movements is 0,848 meaning that the average ICC of the EasyAngle shows good reliability(103) for the movements performed in this study (103).

Appendix 32: Conclusions: intra-rater reliability.

Intra-rater reliability showed excellent reliability in seven movements (flexion, extension, lateral flexion left and right, rotation left and upper cervical rotation left and right) with an ICC higher than 0,9, good reliability was found in one movement (rotation right) (ICC ranging between 0,75 and 0,9) and one movement showed moderate reliability (TMJ opening) (ICC ranging between 0,5 and 0,75)(103). Each ICC score showed to be significant. The average ICC of all movements is 0,906 meaning that the average ICC of the EasyAngle shows excellent reliability for the movements performed in this study (103).

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ABSTRACT IN LAYMAN'S TERMS:

Tinnitus kan begeleid worden door bijkomende problemen die het beperkend maken, deze noemen wij tinnitus-gerelateerde invaliditeit (TRD). Onderzoek heeft zich vooral gericht op klinische evaluaties van spier- en gewrichtsfuncties, maar objectieve metingen kunnen van meerwaarde zijn om het verband tussen tinnitus en deze functies te begrijpen. Tinnitus gaat gepaard gaat met chronische pijn, de relatie hiertussen verdient verder onderzoek. Ons doel is om de relaties tussen TRD en functies van de nek en kaak gewrichten in kaart te brengen en de invloed van chronische pijn is hierop. Hiervoor hebben we 42 deelnemers geanalyseerd via twee vragenlijsten. De nek- en kaakfuncties zijn in kaart gebracht via de EasyAngle, en shear wave elastografie. Er werd een lineaire relatie gevonden tussen de bewegingsuitslag van de kaak en TRD. Daarnaast werd er een relatie gevonden tussen de spierspanning van een van de nekspieren in de groep zonder chronische pijn en TRD. Toekomstig onderzoek moet focussen op het verzekeren van kwaliteit van de studie door: (1) meer deelnemers, (2) valide, betrouwbare en gestandaardiseerde meetstrategieën voor tinnitus impact en nek/kaakfuncties gebruiken; (3) het toevoegen van een controlegroep en (4) het aanpassen van de inclusie criteria om een populatie te krijgen met meer vergelijkbare tinnitus kenmerken.

PROOF OF SUBMISSION TO THE ETHICAL COMITY:

Afz.: Commissie voor Medische Ethiek

Prof. Dr. Mira Meeus
VG Revalidatiewetenschappen
ALHIER

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Ons kenmerk	Uw kenmerk	datum	pagina
BC-07036 E21	NVT	01/07/2021	1/3

Betreft : Advies voor monocentrische studie met als titel:

Titel hoofdstudie: "Modulating mechanisms in patients with chronic subjective tinnitus and/or chronic pain."

Titel thesis: De opsporing van centrale sensitisatie bij chronische pijn: een uitdaging voor elke clinicus. Scriptie Simon Van de Velde

B.U.N.: B6702021000678

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- Alle goedgekeurde documenten van studie met als referentie   BC-07036
- Adviesaanvraagformulier dd. 17-06-2021 (Ontvangen op 23/06/2021)

Advies werd gevraagd door: Prof. Dr. Mira Meeus

BOVENVERMELDE DOCUMENTEN WERDEN DOOR HET ETHISCH COMITÉ BEOORDEELD. ER WERD EEN POSITIEF ADVIES GEGEVEN OVER DIT PROTOCOL OP 30/06/2021 . INDIEN DE STUDIE NIET WORDT OPGESTART VOOR 30/06/2022, VERVALT HET ADVIES EN MOET HET PROJECT TERUG INGEDIEND WORDEN.
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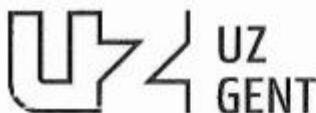* The Ethics Committee stresses that approval of a study does not mean that the Committee accepts responsibility for it. Moreover, please keep in mind that your opinion as investigator is

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Namens het Ethisch Comité / On behalf of the Ethics Committee

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Voorzitter / Chairman

CC: UZ Gent – HIRUZ CTU
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Ledenlijst op 30/06/2021

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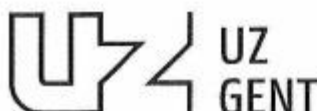Before initiating the study, please contact HIRUZ CTU (09/332 05 00).

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