

COLLAGEN IN THE PATHOLOGIES OF THE MUSCULO-SKELETAL APPARATUS-PAINFUL DISEASES OF JOINT & MUSCLE SYSTEM

IMPORTANT CONTRIBUTION OF COLLAGEN MEDICAL DEVICES



MILANO 16th NOVEMBER 2019

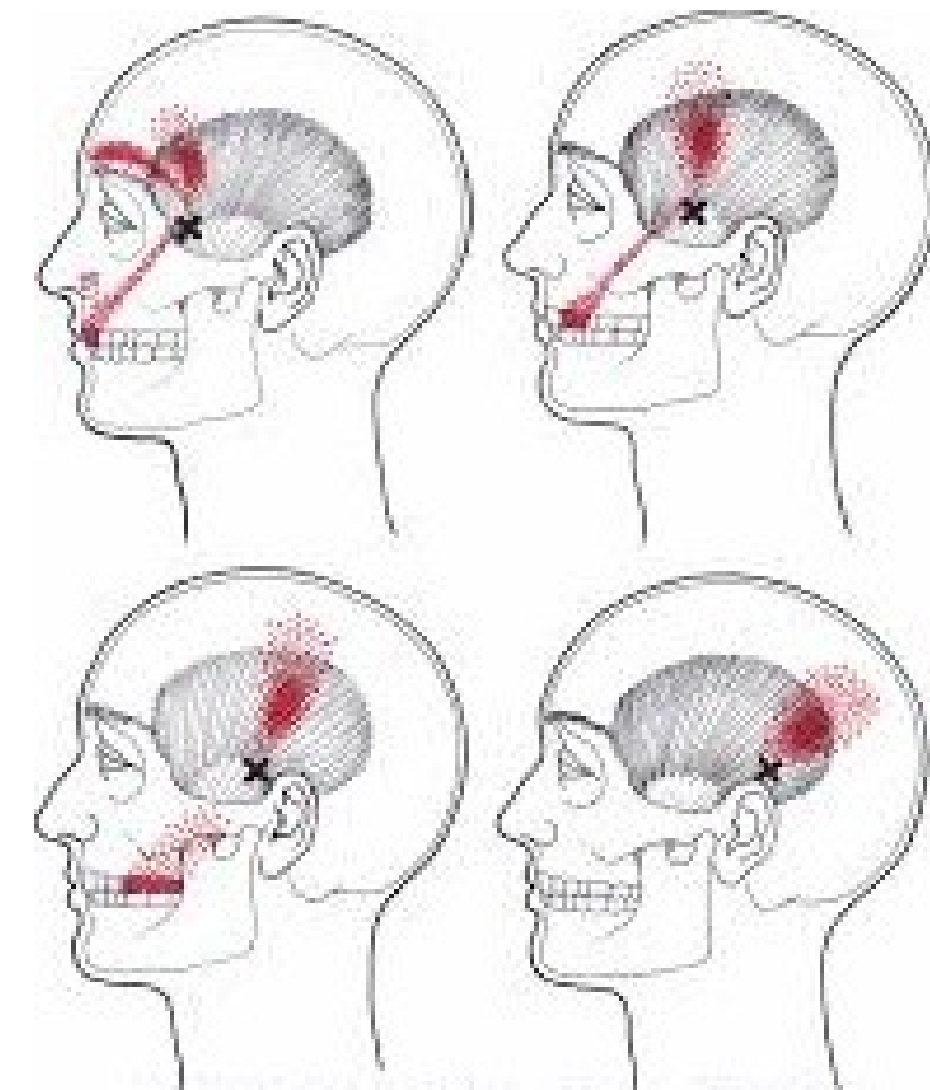
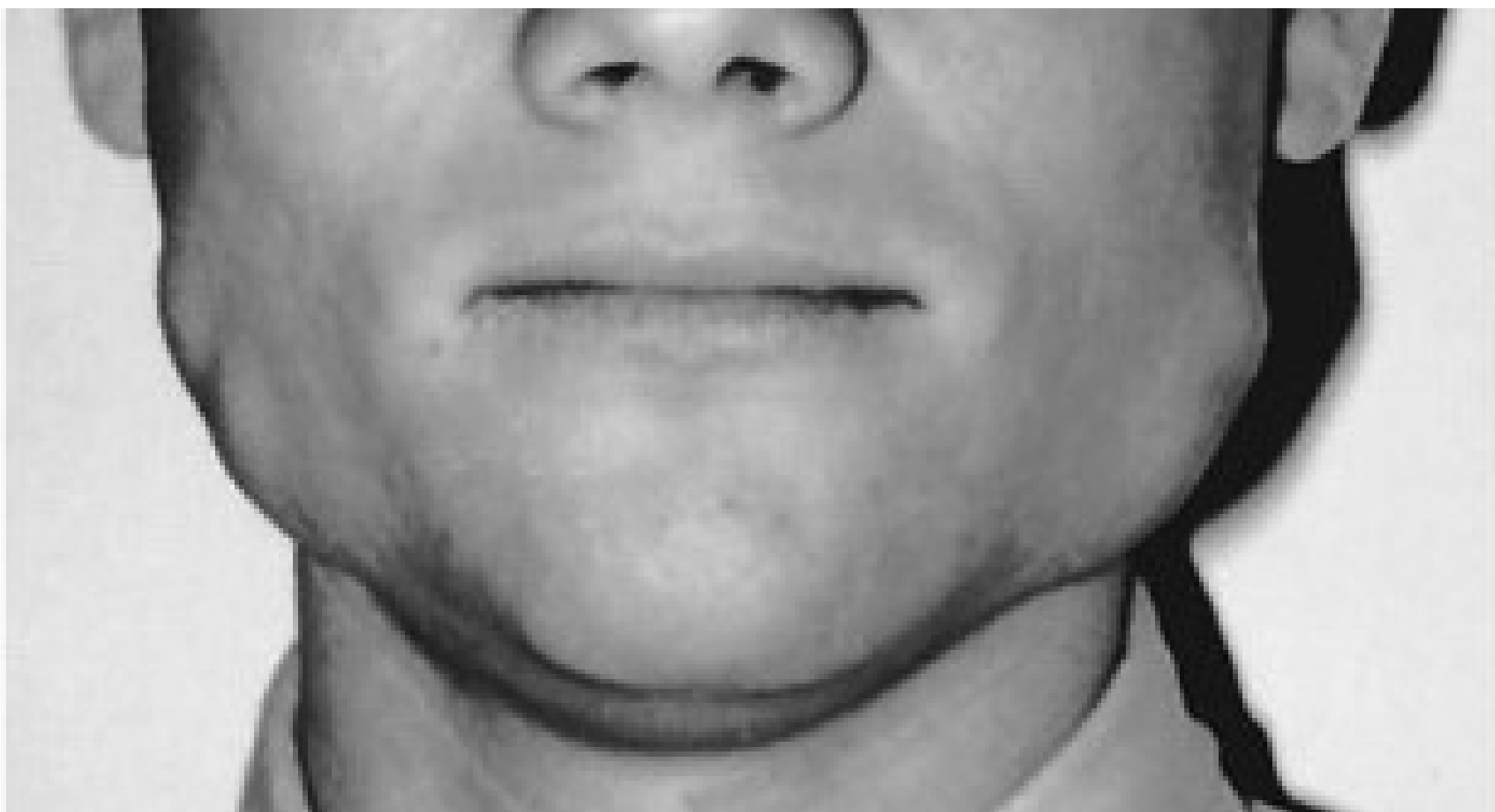
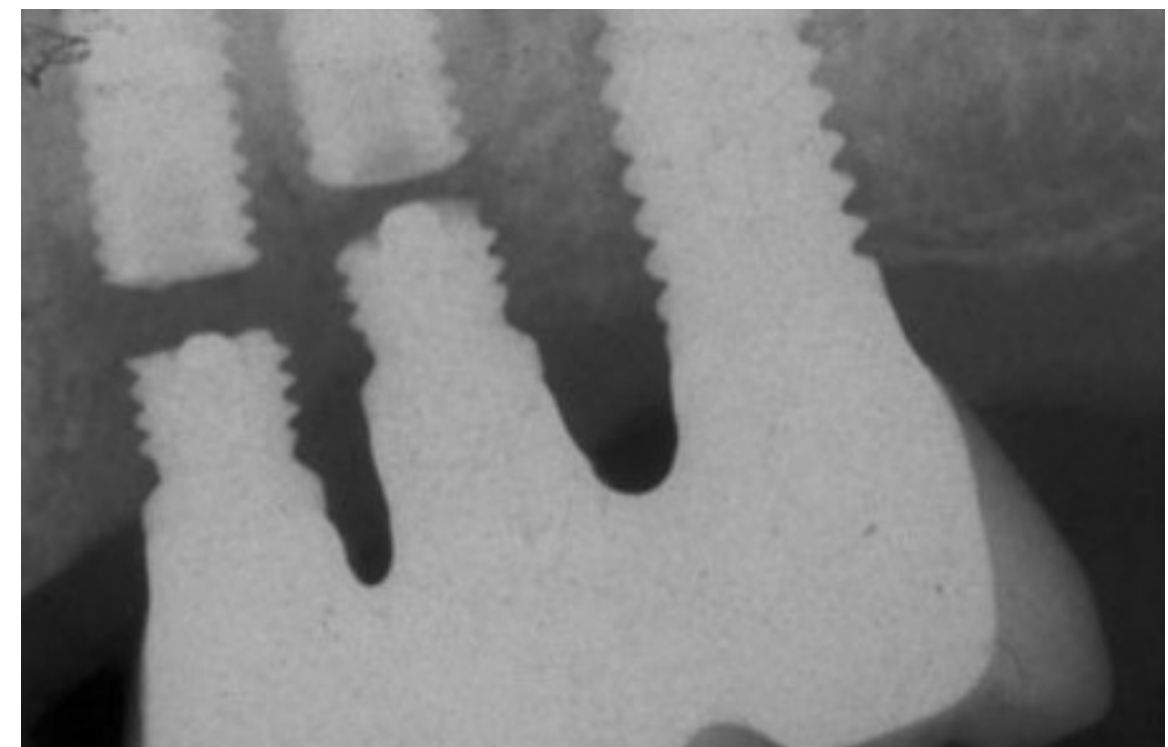
COLLAGEN INTRAMUSCULAR INJECTIONS IN MYOFASCIAL MUSCLE PAIN

ALEKSANDRA NITECKA-BUCHTA*, KAROLINA WALCZYŃSKA-DRAGON, JOLANTA
BATKO-KAPUSTECKA, MIESZKO WIĘCKIEWICZ, STEFAN BARON

POLAND

BRUXISM

BRUXISM MAY LEAD TO EXCESSIVE MUSCLE EFFORT, MASTICATORY MUSCLE HYPERTROPHY, DEVELOPMENT OF MUSCLE PAIN, DAMAGE TO DENTAL HARD TISSUES, FAILURES OF PROSTHODONTIC CONSTRUCTIONS AND HEADACHE*



*Lobbezoo et al. International consensus on the assessment of bruxism: Report of a work in progress. J Oral Rehabil. 2018;45(11):837-844.

M Y A L G I A

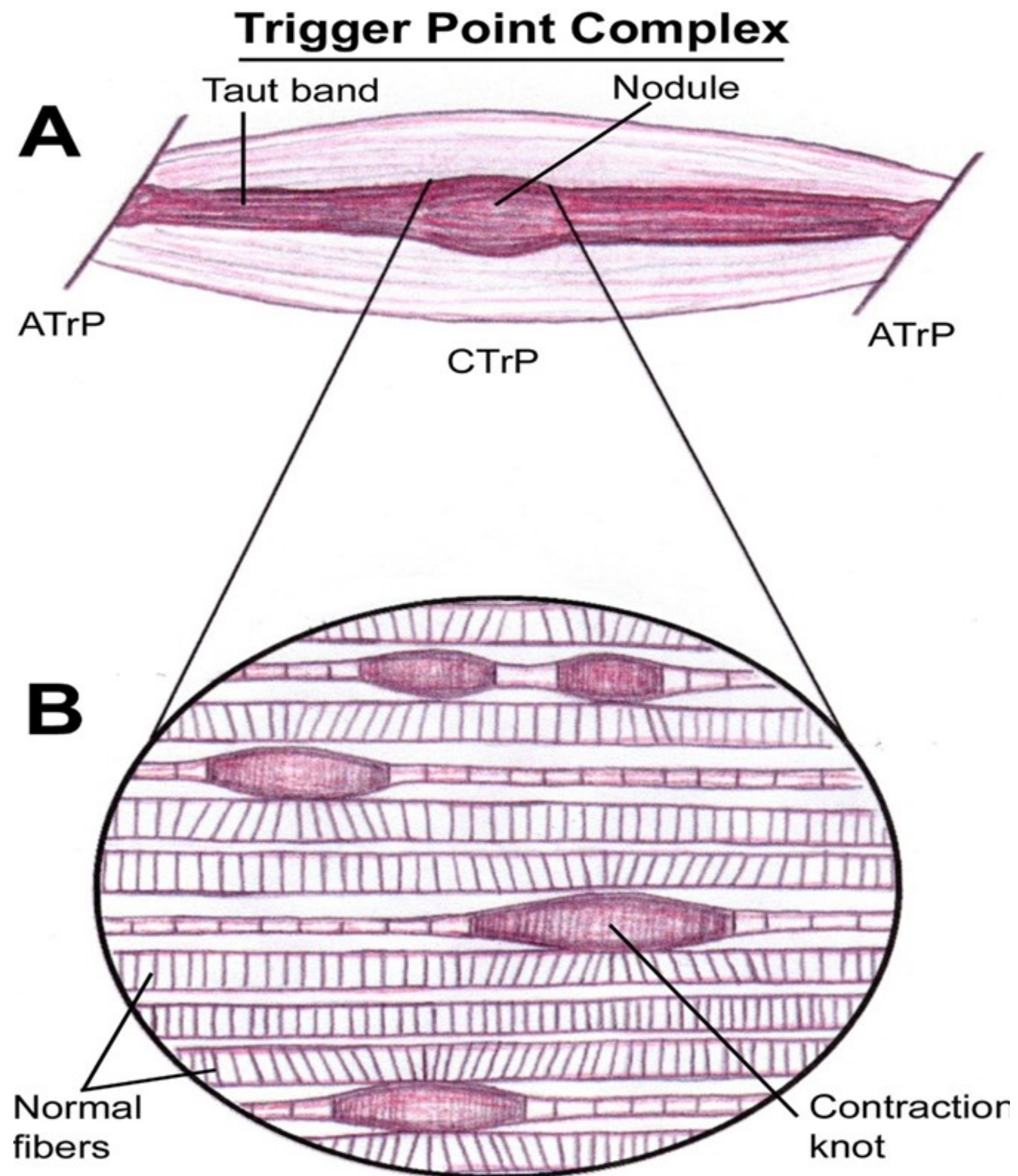
DC/TMD II.1.a 2 and 3*

PRESENCE OF MYOFASCIAL PAIN AND
MYOFASCIAL PAIN WITH REFFERAL
WITHIN MASSETER MUSCLE
(TRIGGER POINTS)

Schiffman et al. Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) for Clinical and Research Applications: recommendations of the International RDC/TMD Consortium Network and Orofacial Pain Special Interest Group†. J Oral Facial Pain Headache. 2014; 28(1): 6-27.

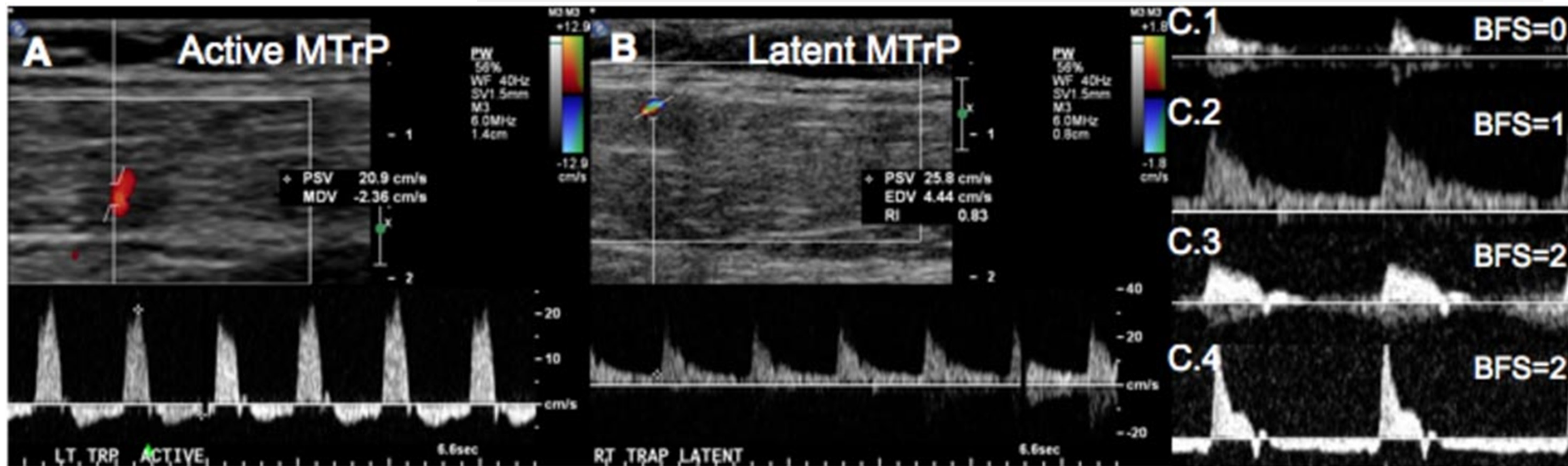
TRIGGER POINT

MAIN CAUSE OF MYOFASCIAL PAIN



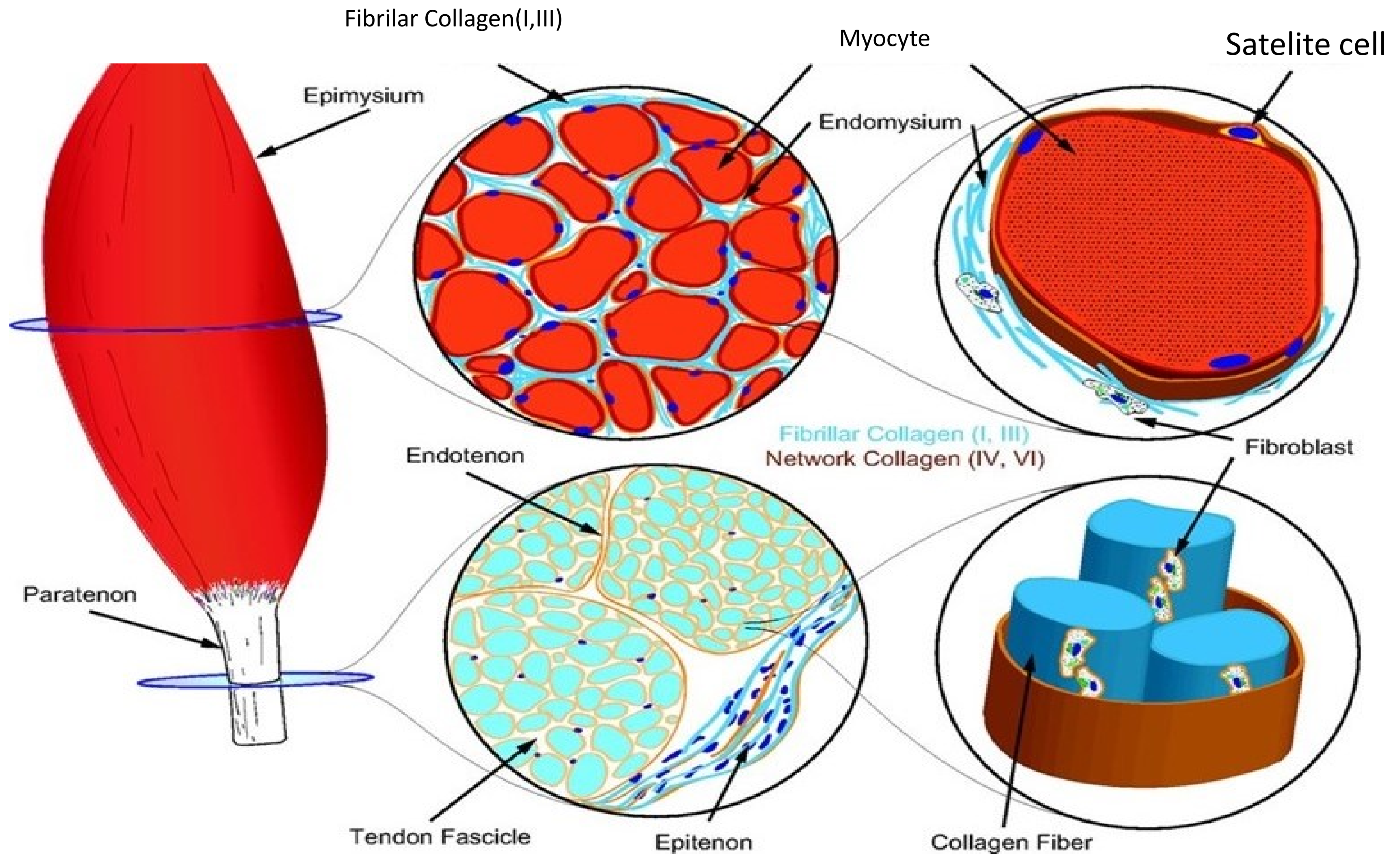
Diagrams from Travel & Simon's
"Myofascial Pain and Dysfunction – The
Trigger Point Manual, Vol. 1 and 2"

3D DOPPLER IN TRIGGER POINT EXAMINATION



Sikdar S. et al. Novel applications of ultrasound technology to visualize and characterize myofascial trigger points and surrounding soft tissue. Arch Phys Med Rehabil. 2009 Nov;90(11):1829-38. doi: 10.1016/j.apmr.2009.04.015

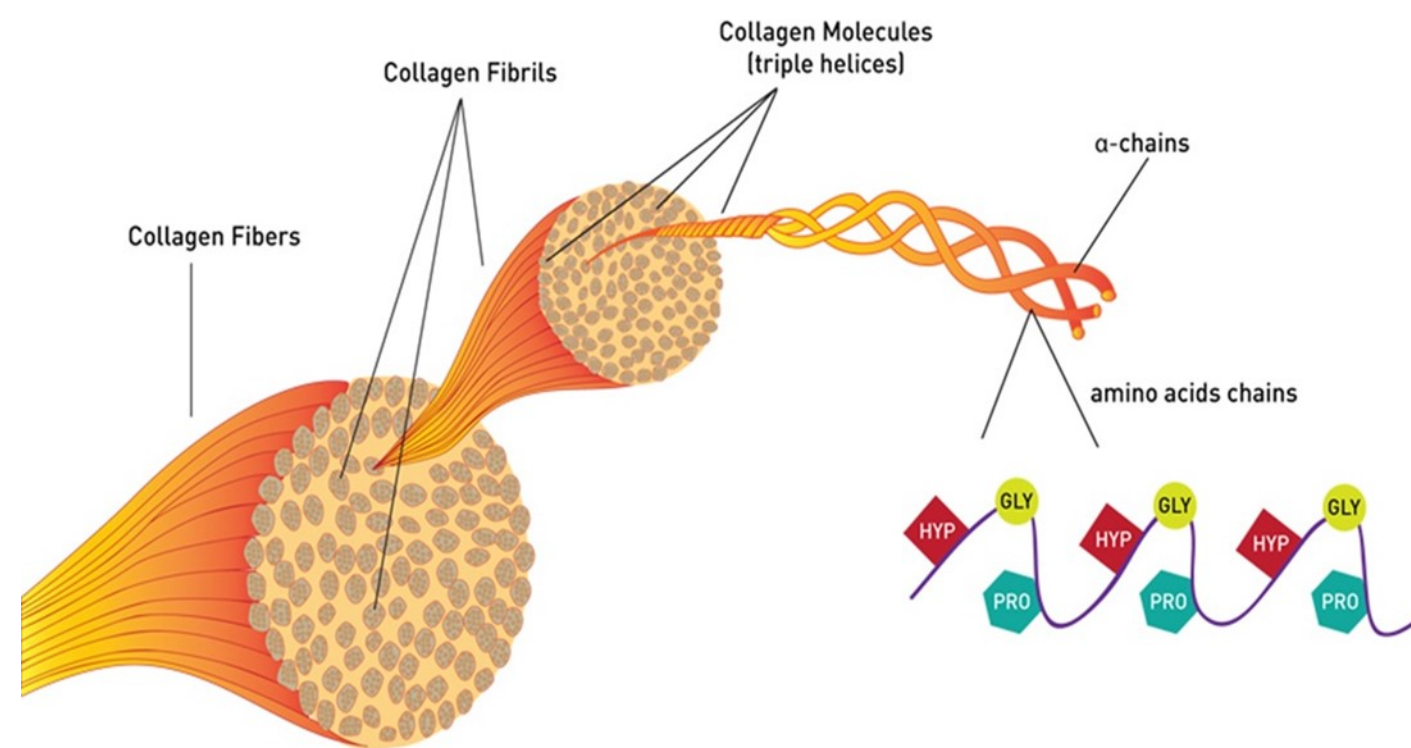
COLLAGEN IN SKELETAL MUSCLES



Max E. Davis, Jonathan P. Gumucio, Kristoffer B. Sugg, Asheesh Bedi, Christopher L. Mendias MMP inhibition as a potential method to augment the healing of skeletal muscle and tendon extracellular matrix *Journal of Applied Physiology* Published 15 September 2013 Vol. 115 no. 6, 884-891 DOI: 10.1152/jappphysiol.00137.2013

COLLAGEN PRODUCTION

INTERSTITIAL FIBROBLASTS CELLS



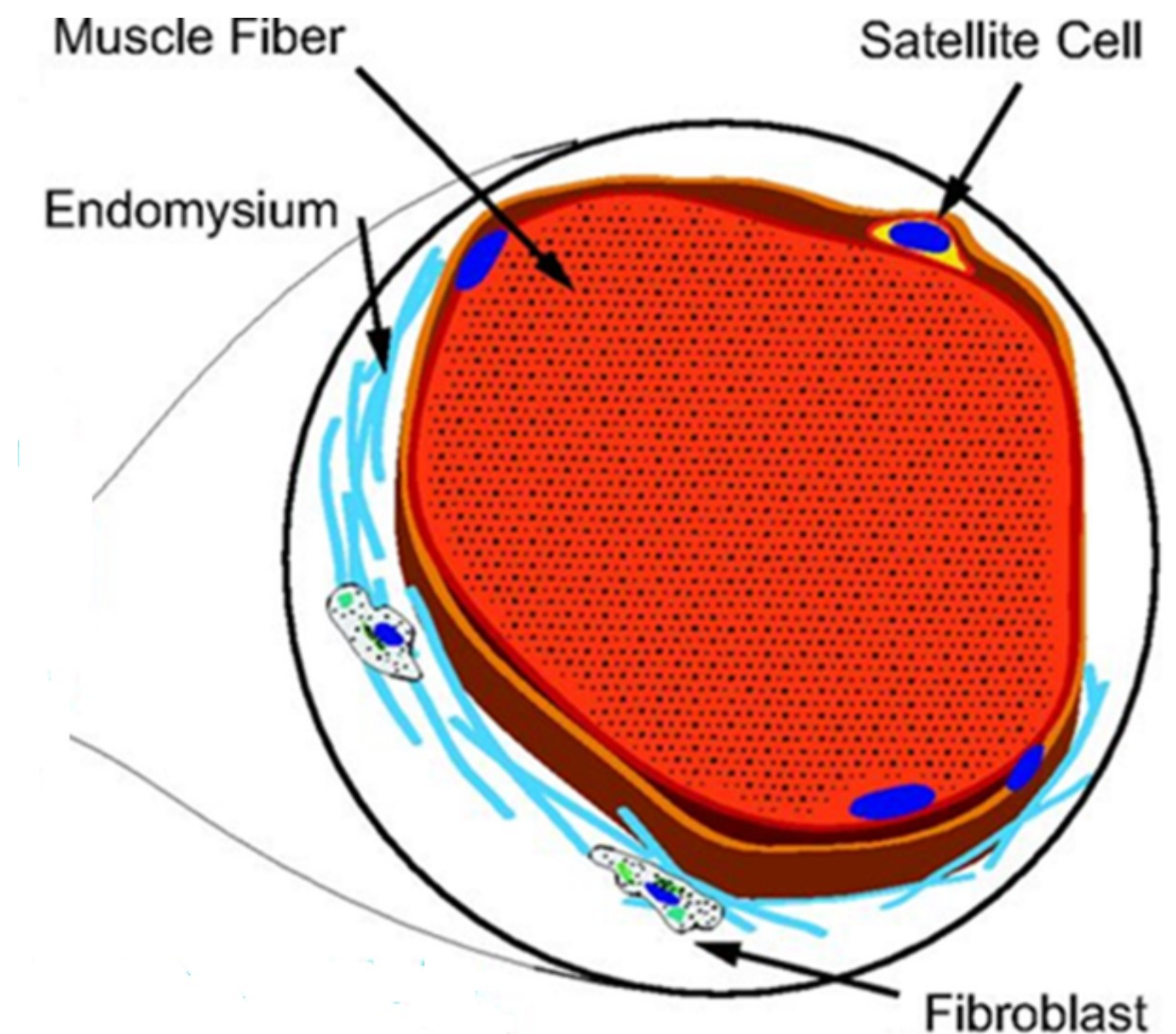
SYNTHETIZE COLLAGEN:

I, III- ENDOMYSIUM,

VI-PERIMYSIUM

**SECRETE COLLAGEN TO THE EXTRACELLULAR
MATRIX**

ACTIVE DURING MUSCLE REGENERATION

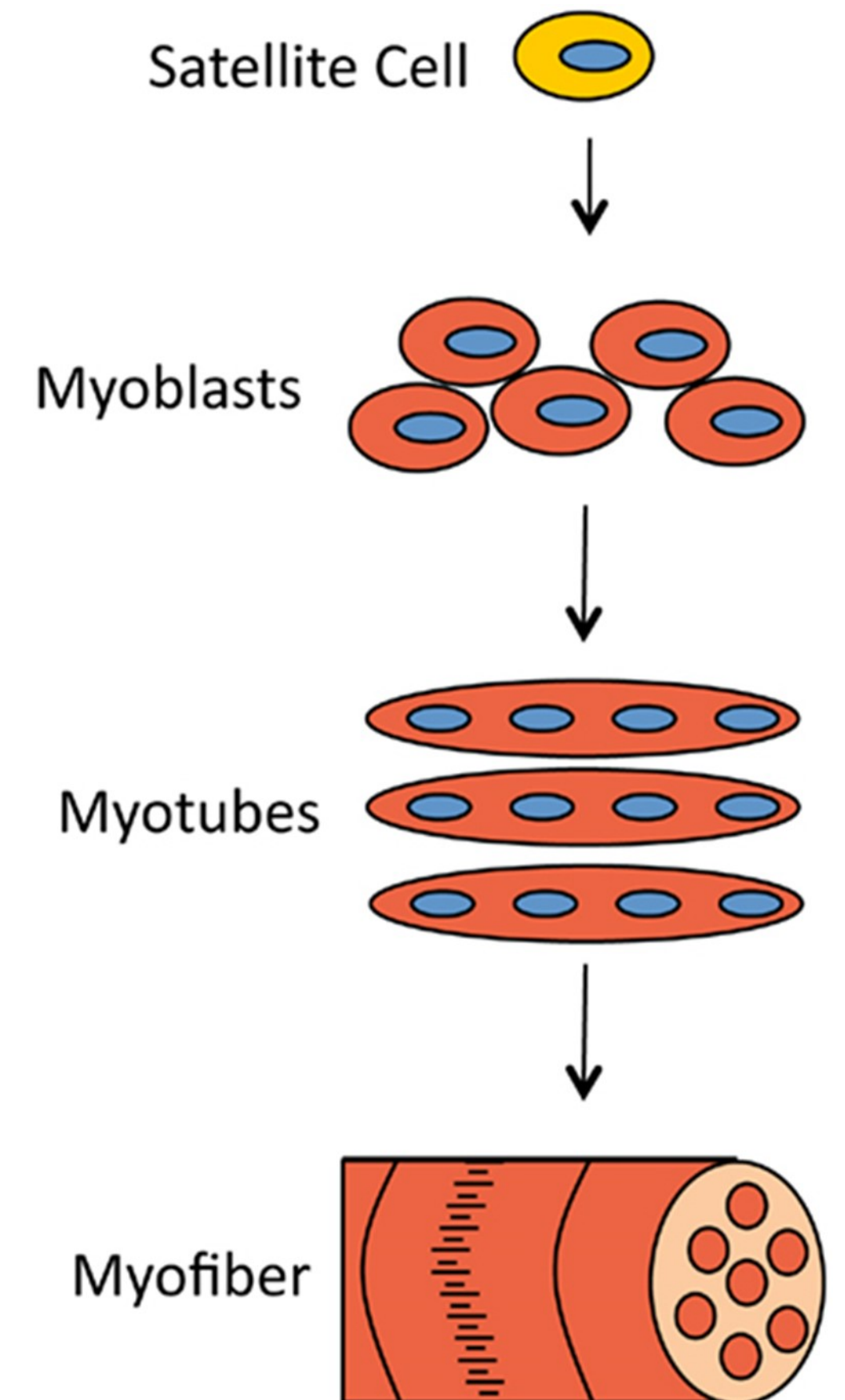


STAGES OF MUSCLE REGENERATION

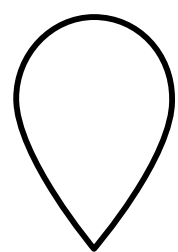
I. MYOFIBER BREAKDOWN AND INFLAMMATION

II. STEM CELL ACTIVATION AND PROLIFERATION

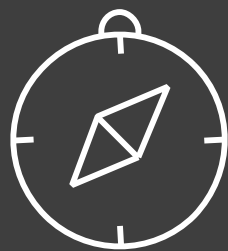
III. DIFFERENTIATION INTO NEW MYOFIBERS –
NEW MUSCLE TISSUE NOT A SCAR



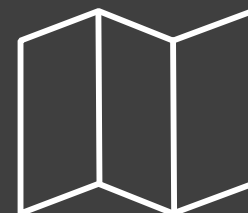
April K. Marrone and Halyna R. Shcherbata* [2011.00064](#) Dystrophin orchestrates the epigenetic profile of muscle cells via miRNAs Front. Genet., 13 September 2011 | <https://doi.org/10.3389/fgene>. Max Planck Research Group of Gene Expression and Signaling, Max Planck Institute for Biophysical Chemistry, Goettingen, Germany



METHODOLOGY



TREATMENT



RESULTS



DISCUSSION

THE STUDY WAS APPROVED BY THE BIOETHICAL COMMITTEE OF
MEDICAL UNIVERSITY OF SILESIA, KATOWICE, POLAND

KNW/0022/KB1/61/I/15

THE STUDY WAS REGISTERED AT CLINICALTRIALS.GOV

NCT03323567

AIM OF THE STUDY

Evaluation of the efficiency
of intramuscular injections
of collagen and lidocaine
in decreasing MFP
within masseter muscles

STUDY PARTICIPANTS

INCLUSION CRITERIA

- (1) Age ≥ 18 and ≤ 60
- (2) Myofascial pain and myofascial pain with referral within masseter muscles (DC/TMD) (II.1.A. 2 and 3)
- (3) Trigger points within masseter muscles under palpation
- (4) Patients' agreement

EXCLUSION CRITERIA

- (1) Orthodontic treatment
- (2) Edentulous patients
- (3) Analgesic drugs, drugs affecting muscle function
- (4) Drug and/or alcohol addiction
- (5) Head and neck traumas (previous 2 years)
- (6) Neurological disorder
- (7) Radiotherapy
- (8) Pain of dental origin
- (9) Pregnancy or lactation
- (10) Malignancy
- (11) Severe mental disorders
- (12) Contraindications for injection therapy
- (13) Patients with needle phobia
- (14) Hypersensitivity to collagen

STUDY DESIGN

- **CONSORT STATEMENT**
- **THE DECLARATION OF HELSINKI**
- **THE INTERNATIONAL CONFERENCE ON HARMONISATION:
GUIDELINES FOR GOOD CLINICAL PRACTICE**
- **PATIENTS GAVE THEIR CONSENT TO PARTICIPATE IN THE STUDY**
- **RANDOMIZED, CONTROLLED , SINGLE BLIND, THREE-ARM TRIAL**
- **10th JANUARY 2016 - 12th DECEMBER 2017**

FLOWCHART OF THE STUDY PROTOCOL

Enrollment

Assessed for eligibility
(n = 102)

Excluded (n = 52)
Not meeting inclusion criteria (n = 38)
Declined to participate (n = 12)
Other reasons (n = 2)

Randomized (n = 50)

Allocation

Allocated to intervention with
Collagen injection (Group I)
(n = 18)
Received allocated
intervention (n = 15):
- Day 0, 1st injection
- Day 7, 2nd injection

Did not receive allocated
intervention (n = 3)
(patient request)

Allocated to intervention with
Lidocaine injection (Group II)
(n = 15)
Received allocated intervention
(n = 13):
- Day 0, 1st injection
- Day 7, 2nd injection

Did not receive allocated
intervention (n = 2)
(patient request)

Allocated to intervention with
control injection (Group III)
(n = 17)
Received allocated
intervention (n = 15):
- Day 0, 1st injection
- Day 7, 2nd injection

Did not receive allocated
intervention (n = 2)
(patient request)

Follow up

Examined:
- Day 0, n=15
- Day 7, n=15
- Day 14, n=15
Lost to follow up
(n = 0)

Examined:
- Day 0, n=13
- Day 7, n=13
- Day 14, n=13
Lost to follow up
(n = 0)

Examined:
- Day 0, n=15
- Day 7, n=15
- Day 14, n=15
Lost to follow up
(n = 0)

Analysis

Analyzed (n = 15)

Excluded from analysis
(n = 0)

Analyzed (n = 13)

Excluded from analysis
(n = 0)

Analyzed (n = 15)

Excluded from analysis
(n = 0)

GROUP CHARACTERISTICS

COLLAGEN

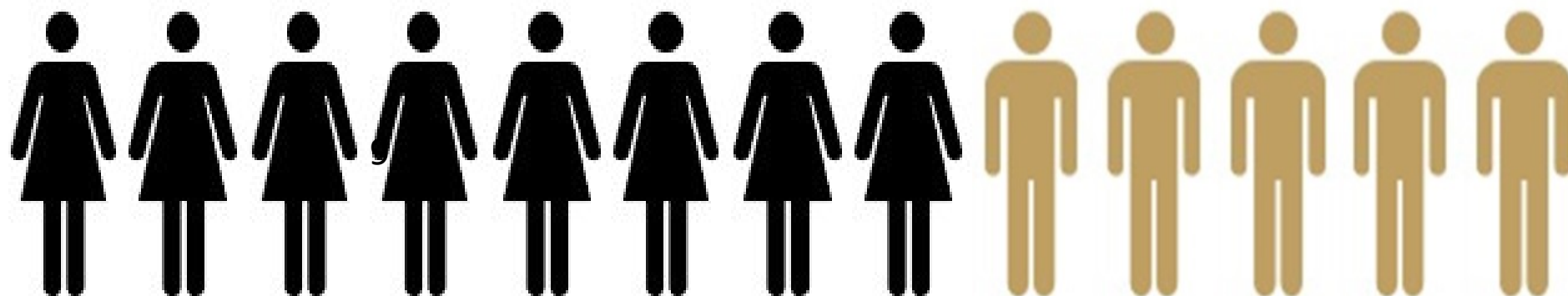


37,2 YEARS
(SD=4,97)

30,2 WEEKS OF PAIN (SD=31,48)



LIDOCAINE

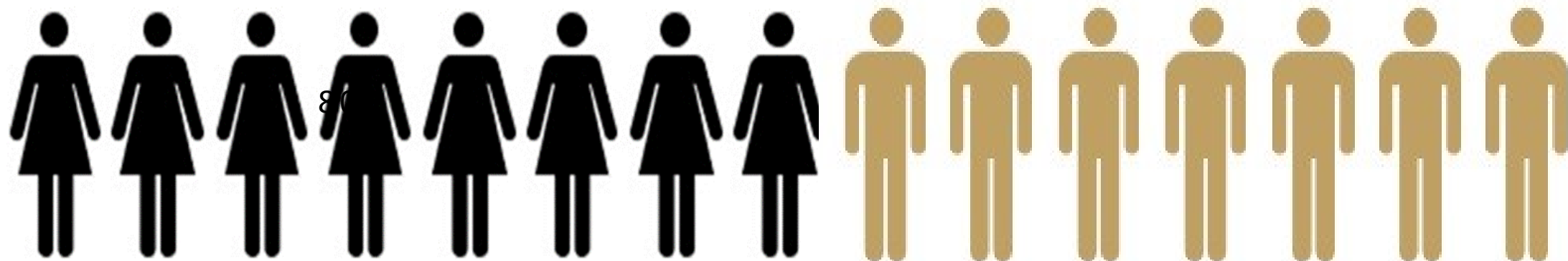


42,8 YEARS
(SD=0,98)

34,3 WEEKS OF PAIN (SD=29,26)



SALINE



40,3 YEARS
(SD=1,18)

38,3 WEEKS OF PAIN (SD=26,47)



CLINICAL TRIAL VISITS



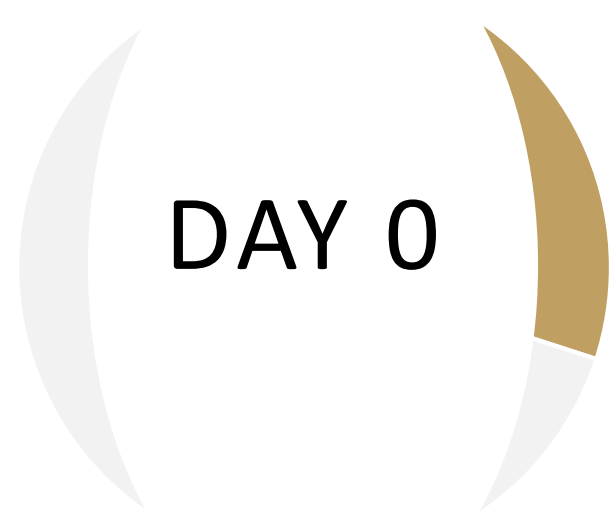
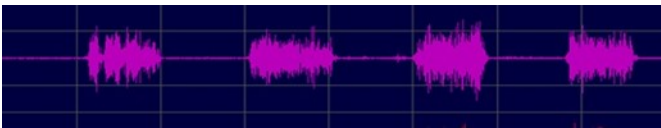
SCREENING
FOR THE STUDY
PARTICIPATON
AND INCLUSION



1ST FOLLOW-UP VISIT
SECOND INJECTION OF
COLLAGEN, LIDOCAINE , SALINE
VAS SCALE



sEMG MEASUREMENT



BASELINE VISIT
FIRST INJECTION OF
COLLAGEN, LIDOCAINE,
SALINE



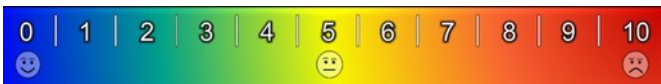
VAS SCALE



sEMG MEASUREMENT



2ND FOLLOW-UP VISIT



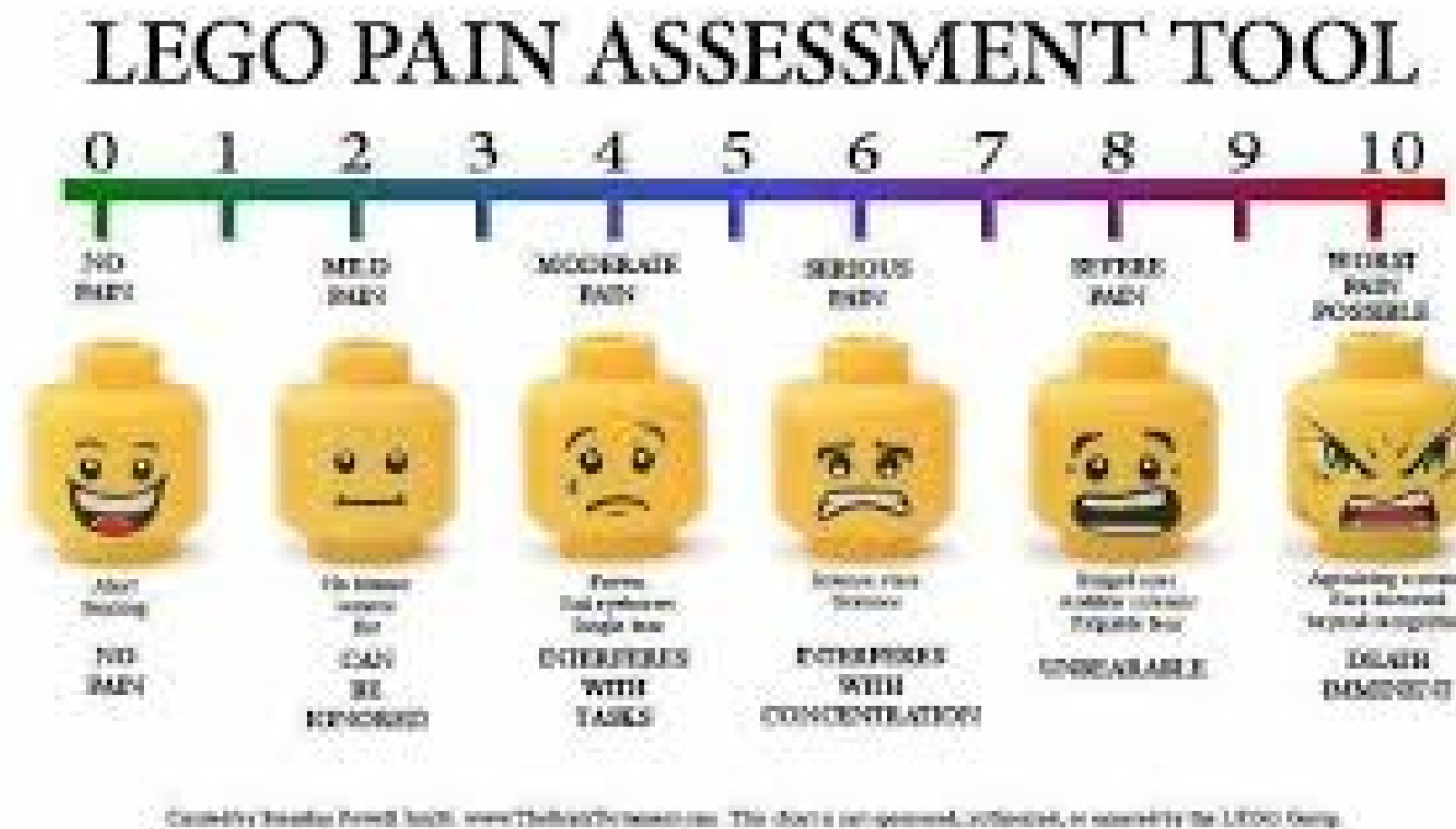
VAS SCALE



SEMG MEASUREMENT,

PRIMARY TREATMENT OUTCOME

PAIN ASSESMENT IN VAS SCALE



PATIENTS SUBJECTIVE INDIVIDUAL OPINION

PAIN EVALUATION WAS PERFORMED BY BLINDED INVESTIGATOR

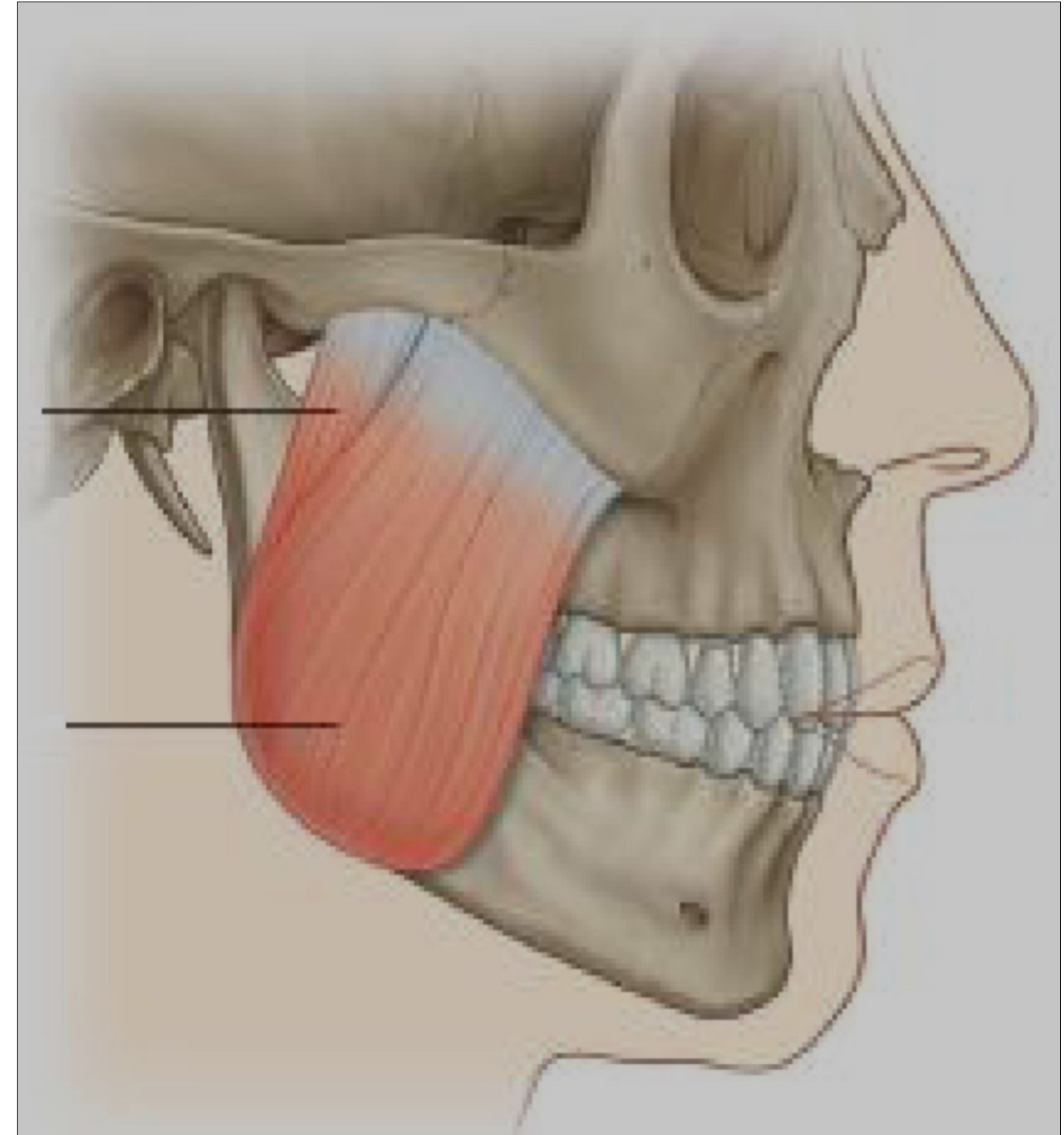
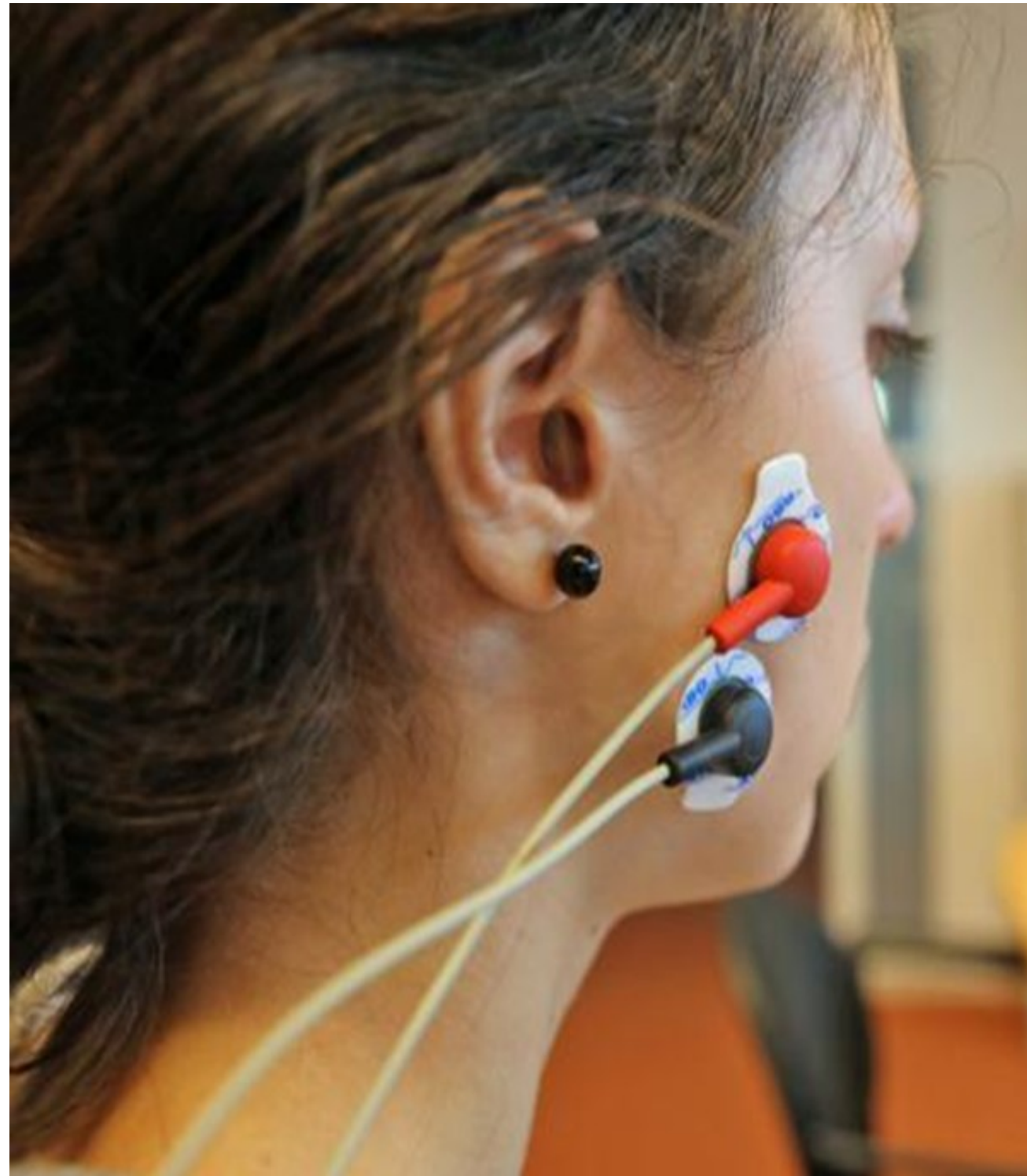
0-10 VISUAL ANALOGUE SCALE WITH THE END-POINTS MARKED „NO PAIN” - 0, WORSE EXPERIENCED PAIN” - 10



SECONDARY TREATMENT OUTCOME

EVALUATION OF MASSETER MUSCLE SURFACE ELECTROMYOGRAPHIC ACTIVITY

ACCORDING TO SENIAM GUIDELINES,
SELF ADHESIVE GEL ELECTRODES, REFERENCE ELECTRODE ON THE NECK BILATERALLY





SURFACE ELECTROMYOGRAPHY

NEUROBIT OPTIMA 4.0

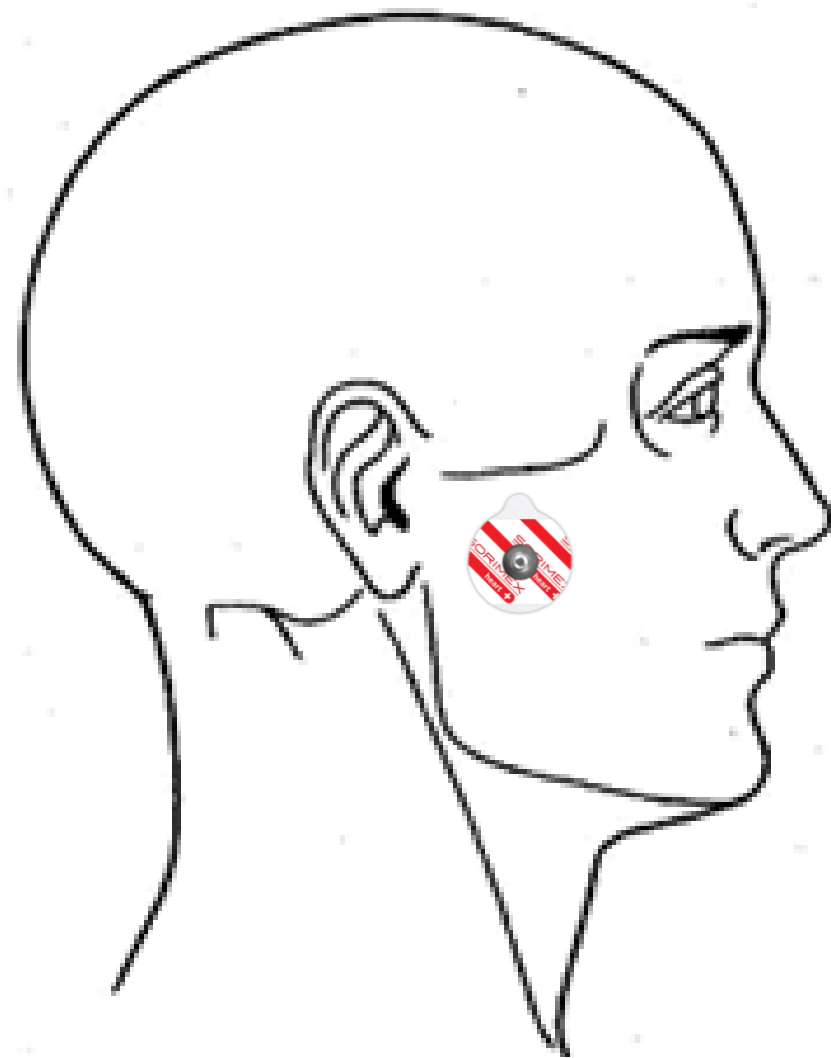
NEUROBIT SYSTEM, POLAND

- REST VALUES FOR BOTH SIDES
- SEMG ACTIVITY WAS MEASURED 3 TIMES
- MEAN VALUES WERE COLLECTED
- REFERENCE ELECTRODE ON THE NECK
- 2-4 VERSATILE,
- ACCURATE,
- LOW NOISE MEASUREMENT CHANNELS
- BIOEXPLORER SOFTWARE

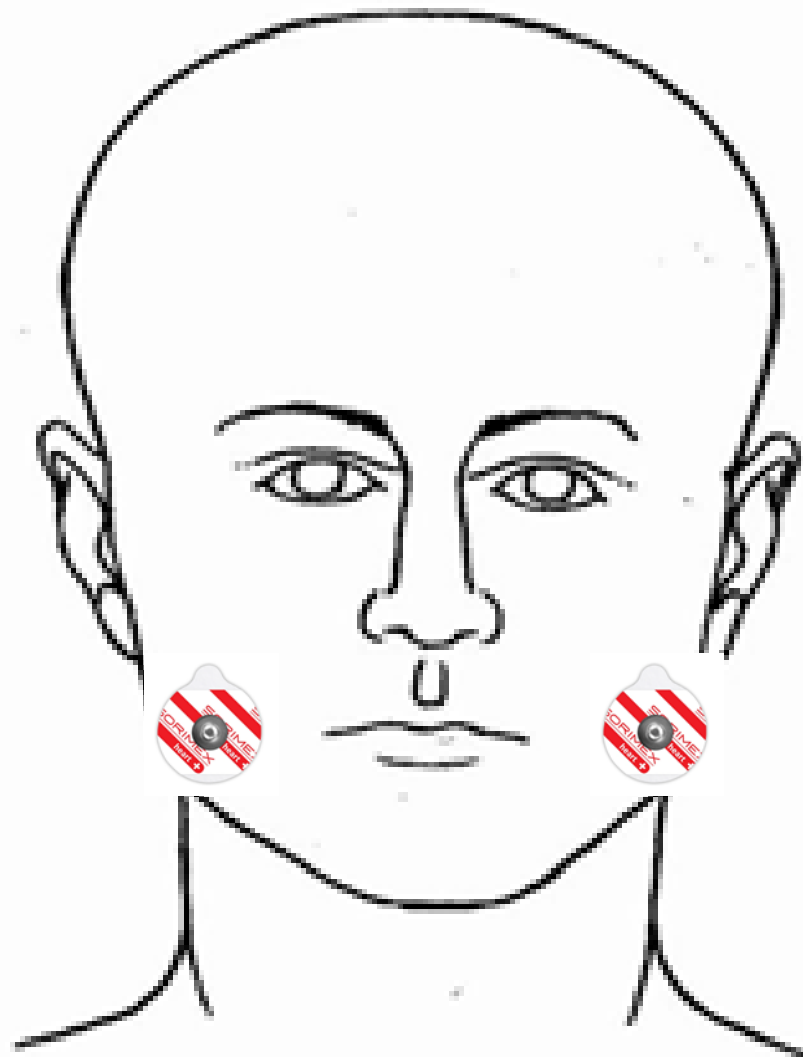
PLACEMENT OF THE ELECTRODES

Five Ag/AgCl adhesive electrodes, diameter 30 mm (Sorimex, Poland).

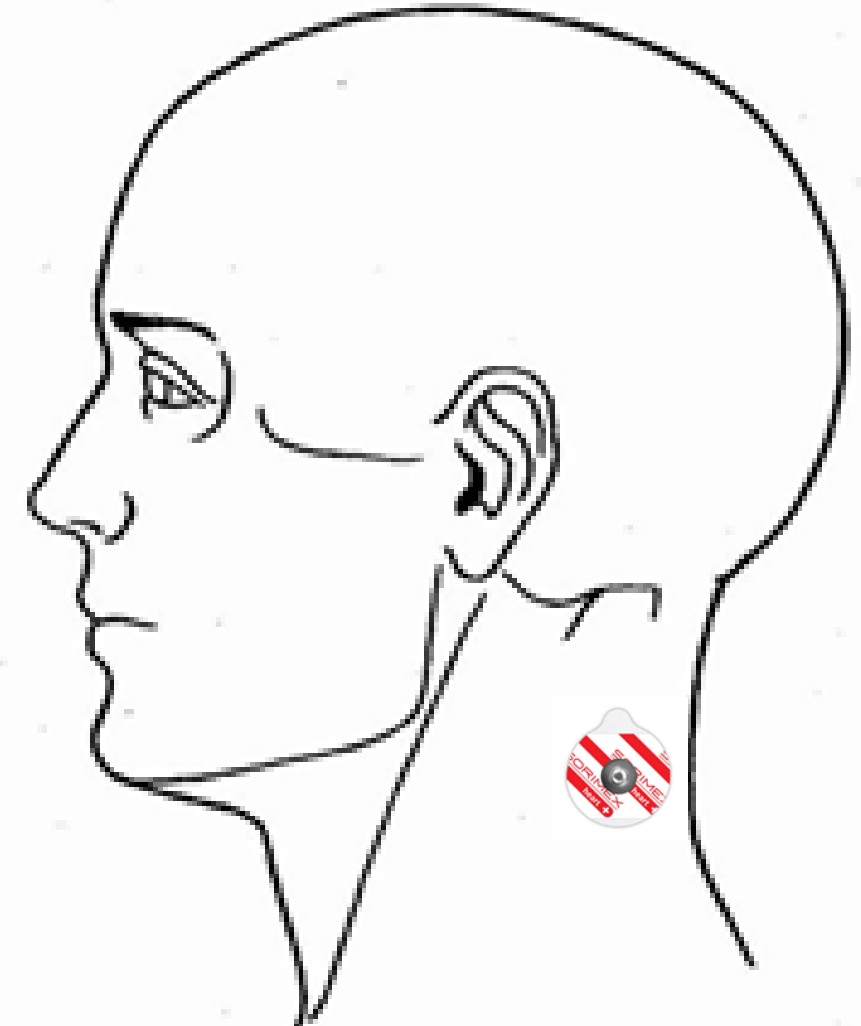
SENIAM guidelines: facial hair was shaved if necessary and cleaned with alcohol.



**UNDER THE
ZYGOMATIC ARCH**



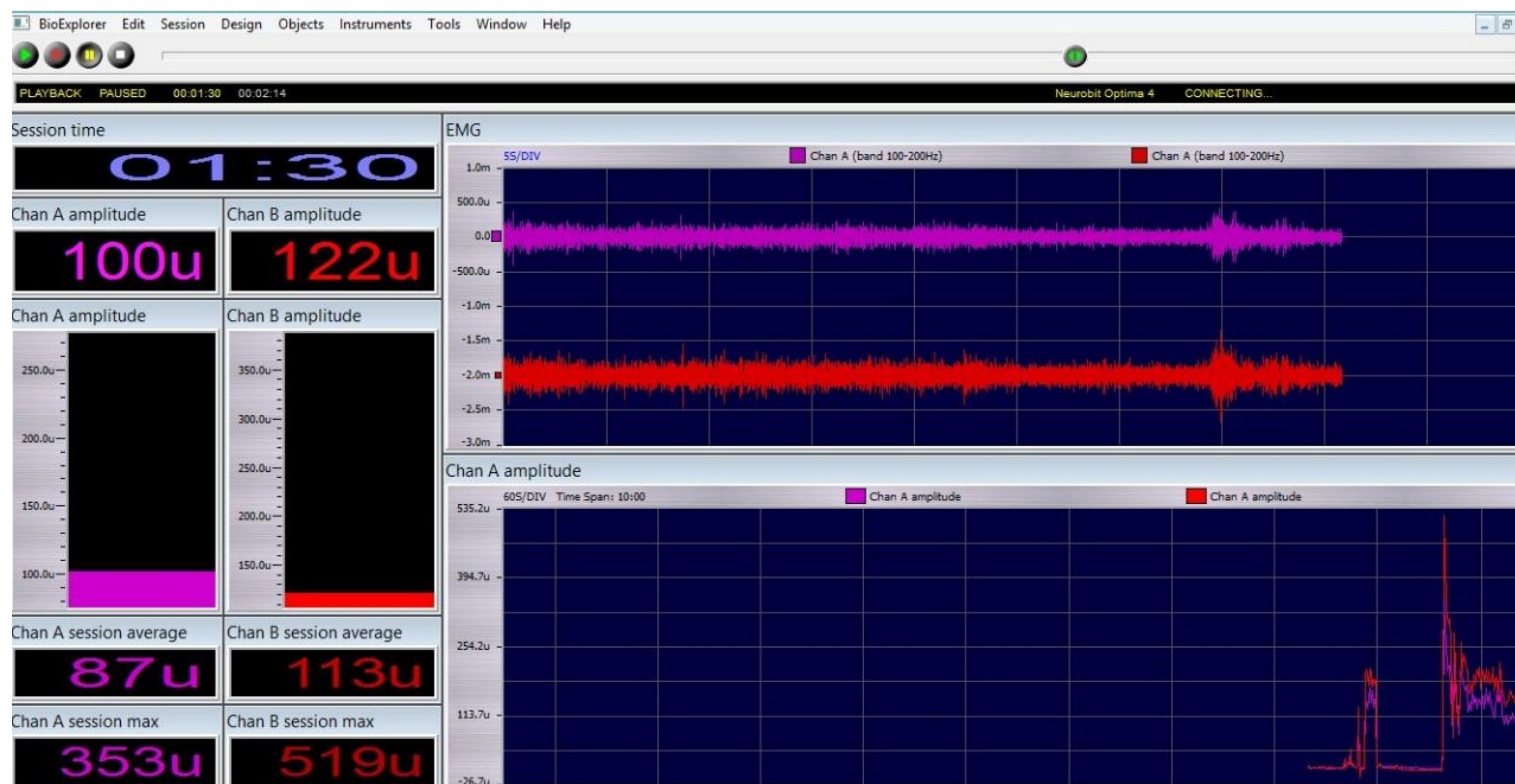
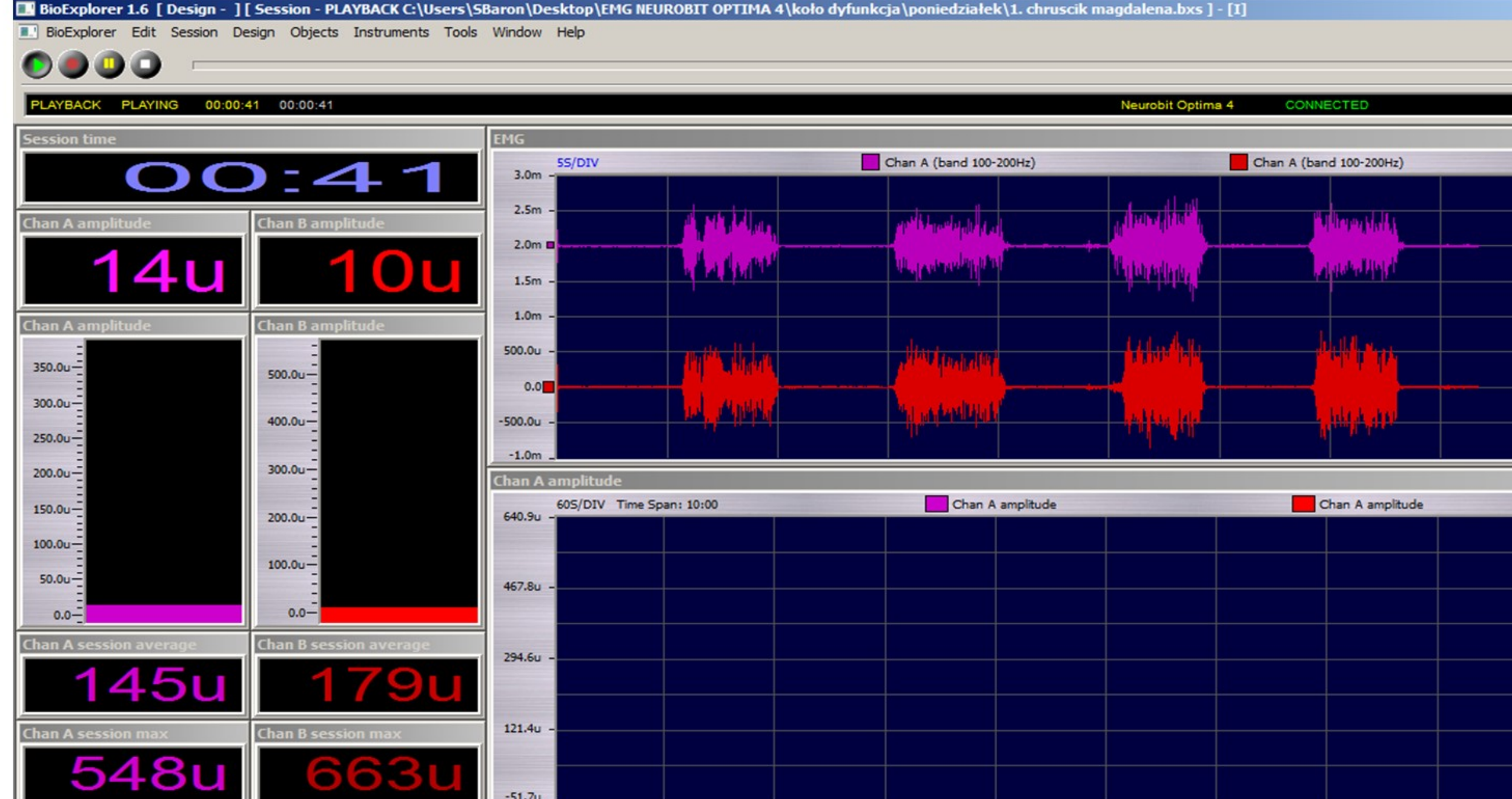
**ON THE MANDIBLE
ANGLE**



**REFERENCE ELECTRODE
ON THE NECK**

sEMG **BIOEXPLORER** **SOFTWARE 1.6**

sEMG VALUES OF MASSETER MUSC
ON THE RIGHT AND LEFT SIDE
REPETITIVE TOOTH CLENCHNG



sEMG **IN REST** **MANDIBLE** **POSITION**

INCREASED MUSCLE sEMG
ACTIVITY DURING REST
MANDIBLE POSITION AND
IN MAXIMAL CONTRACTION

sEMG REGISTRATION



SAMPLE SIZE ESTIMATION

VAS NORMAL DISTRIBUTION WAS ASSUME

POWER TO ACHIEVE WAS 0.9 WITH LEVEL OF SIGNIFICANCE 0.05

THE TOTAL NUMBER OF SUBJECTS NEEDED WAS 36

MINIMUM 12 SUBJECTS PER GROUP

STATISTICS PERFORMED WITH SAS (INSTITUTE INC.CARY, NC)

LEAR (LINEAR EXPONENT AR(1)) MODEL WAS ADOPTED

STATISTICAL ANALYSIS

Statistica - [Dane: MD MV, LID MV, SAL MV, VAS (18 zmn. * 15 prz.)]

Dodaj do skoroszytu • Dodaj do raportu • Dodaj do MS Word • Wstaw do przestrzeni roboczej •

Arial 10

Plik Edycja Widok Wstaw Format Statystyka Data Mining Wykresy Narzędzia Dane Okno Pomoc

	1 EMG.I.1.	2 EMG.I.2.	3 EMG.I.3.	4 VAS.I.1.	5 VAS.I.2.	6 VAS.I.3.	7 EMG.II.1	8 EMG.II.2	9 EMG.II.3
1	60	32	27	8	4	2	61	45	40
2	58	33	29	7	5	4	59	42	33
3	47	40	29	9	2	5	59	41	31
4	63	31	23	10	3	5	58	39	33
5	59	29	27	8	6	4	63	38	32
6	49	31	22	5	5	5	62	44	45
7	53	30	26	6	4	2	60	40	38
8	57	34	24	9	6	5	55	37	34
9	65	32	21	8	5	2	59	42	37
10	63	36	22	10	3	1	53	38	29
11	57	28	26	9	6	7	62	39	37
12	58	29	26	7	5	3	70	45	40
13	48	30	23	6	3	1	59	49	32
14	63	41	21	9	8	7	49	38	30
15	50	34	20	10	5	3	72	60	55

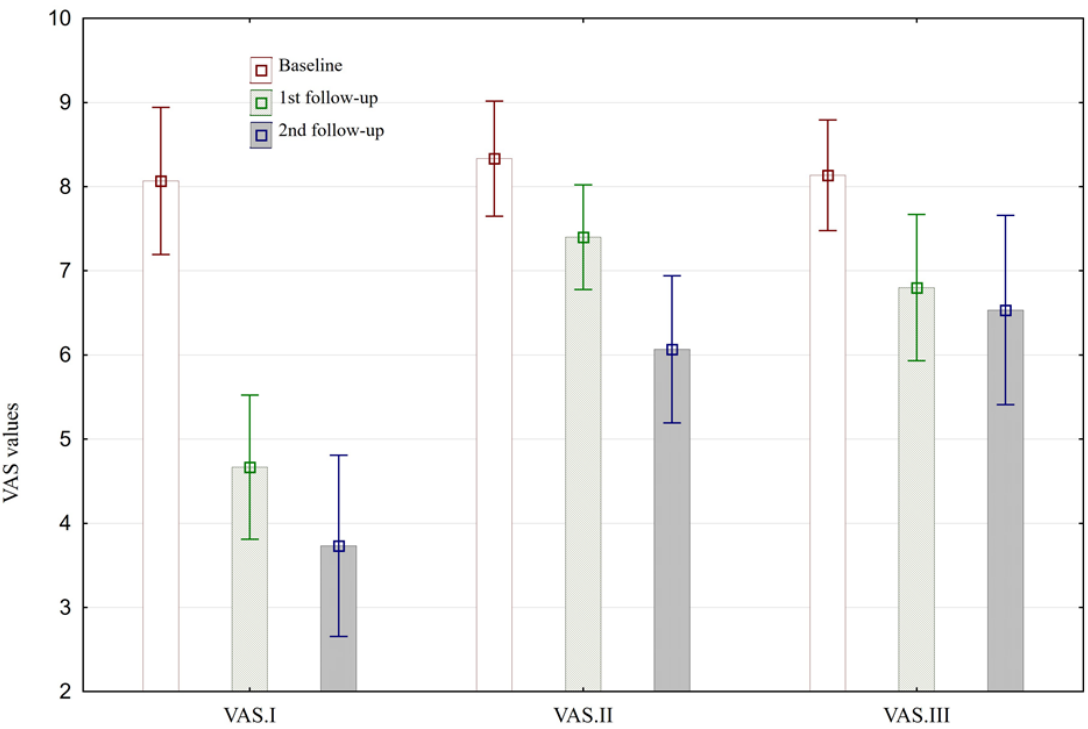
A ONE WAY REPEATED ANALYSIS OF VARIANCE WAS CARRIED OUT

ANALYSIS OF THE NORMALITY OF THE DISTRIBUTION SHAPIRO-WILK TEST

HOMOGENITY OF VARIANCE ANALYZED BY HARTLEY’S TEST, COCHRAN-COX TEST, BARTLETT’S CHI-SQUARE TEST , MAUCHLEY TEST

THE LEVEL OF SIGNIFICANCE WAS ALPHA=0.05

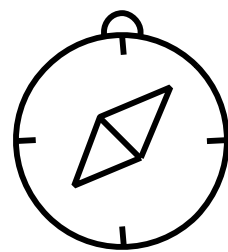
STATISTICA 12.0 (STATSOFT, POLAND)



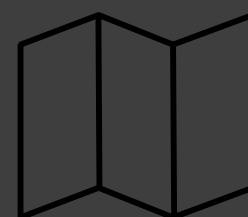
Visit	Group I	Group II	Group III
Baseline	8	8.3	8.13
1 st follow-up visit	4.6	7.4	6.8
2 nd follow-up visit	3.7	6	6.5
VAS changes	-4.3	-2	-1.63
Percentage VAS changes	-53.75%	-25%	-20.1%



METHODOLOGY



TREATMENT



RESULTS



DISCUSSION

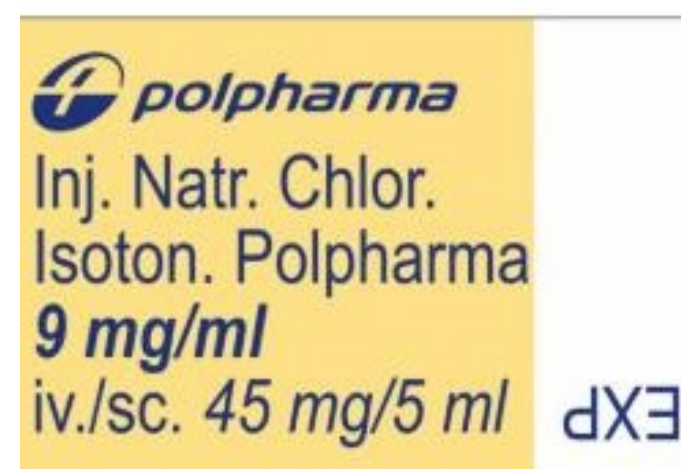
INTRAMUSCULAR INJECTIONS



- **COLLAGEN MD MUSCLE**



- **LIDOCAINUM 2% POLPHARMA**
without vasoconstrictor



- **SALINE 0.9% NaCl POLPHARMA**

SKIN PREPARATION BEFORE INJECTION

THE SKIN OVER MASSETER MUSCLE WAS DISINFECTED, DEGREASED BEFORE INJECTION.

TRIGGER POINTS WERE PALPATED AND HELD BETWEEN OPERATORS FINGERS.

SMALL AMOUNT APRX. 2ml WAS SLOWLY INJECTED INTO THE MUSCLE





0,4mm x 19mm NEEDLE FOR INJECTIONS

BD MICROLANCE



DISPOSABLE SYRINGE

BD DISCARDIT

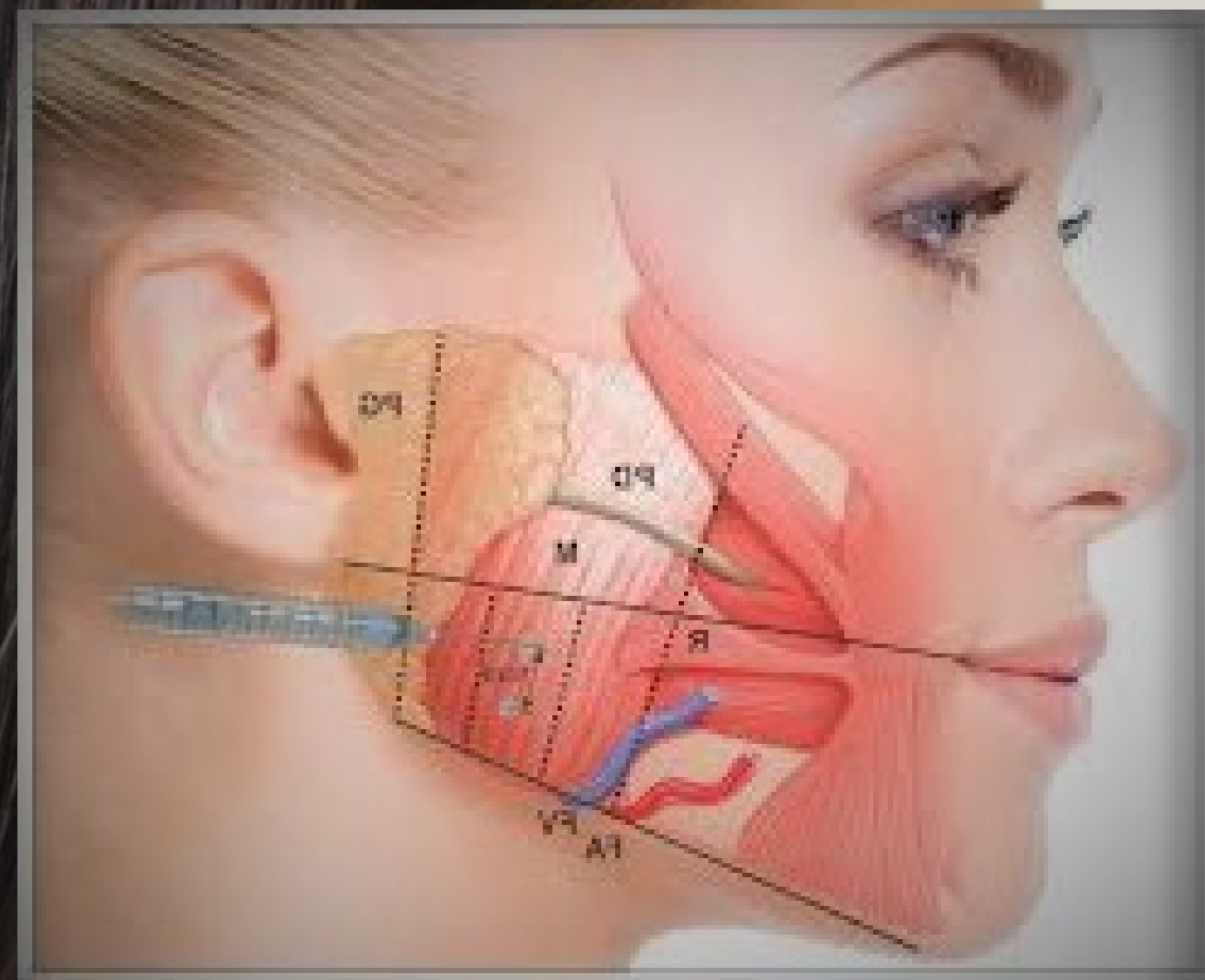
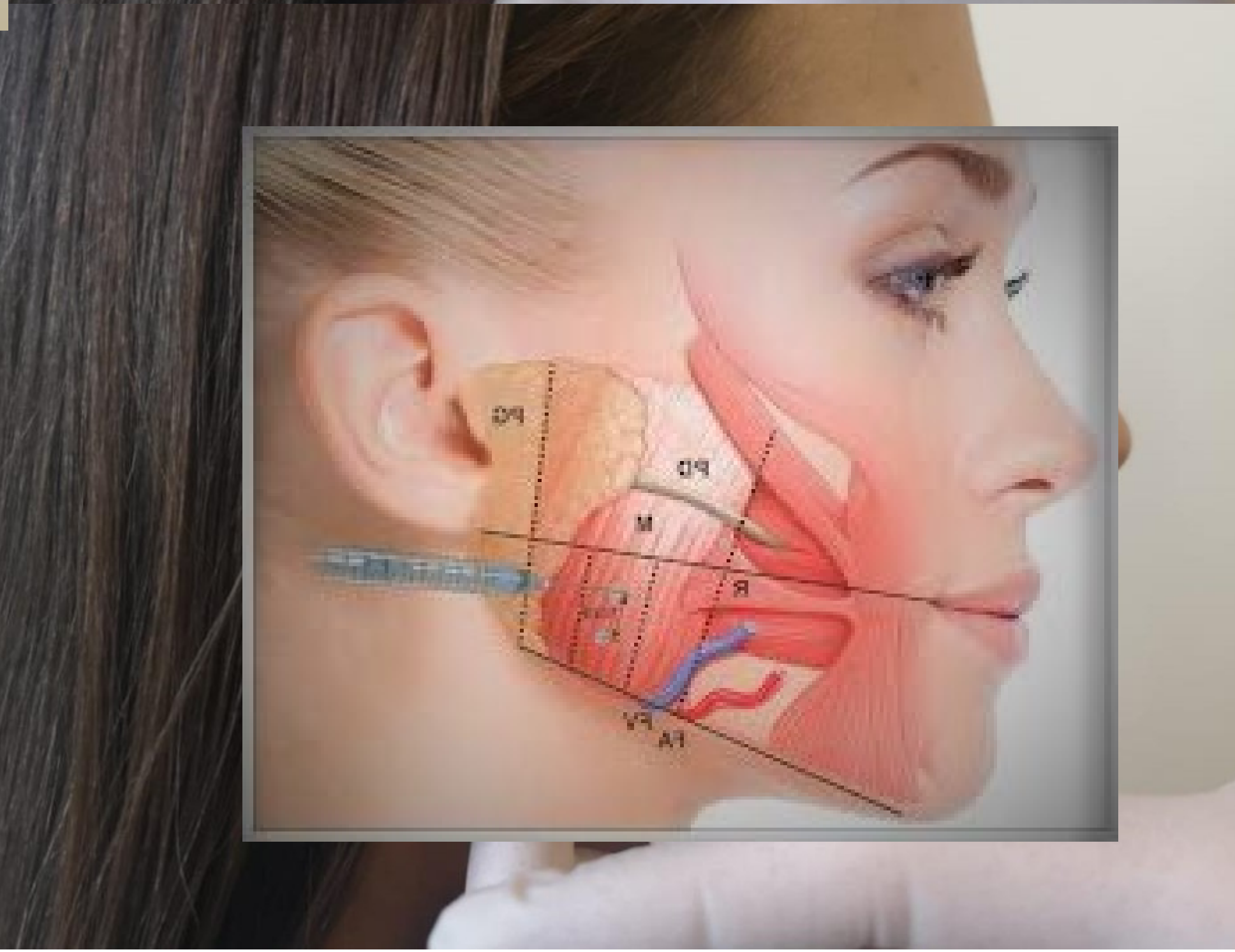


ORIGIN OF MASSETER MUSCLE
TRIGGER POINTS PALPATED

INTRAMUSCULAR INJECTION OF 2 ml

1-1,5 CM UNDER THE SKIN SURFACE

**UNILATERAL IN 40 PATIENTS
BILATERAL IN 3 PATIENTS**



00

BASELINE
VISIT

APRIL 2017						
Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
						1
2	3	4	5	6	7	8
9	10	11	12	13	14 Good Friday	15
16 Easter Sunday	17	18	19	20	21	22
23	24	25	26	27	28	29
30						
My Calendar Land – www.mycalendarland.com						

07

1ST
FOLLOW-UP
VISIT

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
						1
2	3	4	5	6	7	8
9	10	11	12	13	14 Good Friday	15
16 Easter Sunday	17	18	19	20	21	22
23	24	25	26	27	28	29
30						

14

2ND
FOLLOW-
UP VISIT

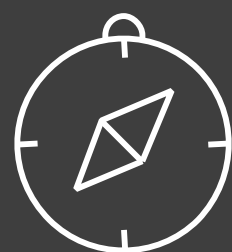
Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
						1
2	3	4	5	6	7	8
9	10	11	12	13	14 Good Friday	15
16 Easter Sunday	17	18	19	20	21	22
23	24	25	26	27	28	29
30						

INTRAMUSCULAR INJECTION COLLAGEN/LIDOCAINE/SALINE

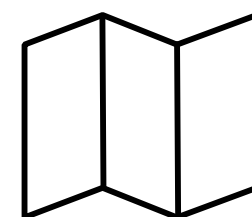




METHODOLOGY



TREATMENT



RESULTS



DISCUSSION

R E S U L T S

PRIMARY TREATMENT OUTCOME: VAS

SECONDARY TREATMENT OUTCOME: sEMG

REDUCTION OF PAIN INTENSITY IN VAS SCALE IN ALL GROUPS

VAS

<i>Visit</i>	<i>Group I</i>	<i>Group II</i>	<i>Group III</i>
<i>Baseline</i>	8	8.3	8.13
<i>1st follow-up visit</i>	4.6	7.4	6.8
<i>2nd follow-up visit</i>	3.7	6	6.5
<i>VAS changes</i>	-4.3	-2	-1.63
<i>Percentage VAS changes</i>	-53.75%	-25%	-20.1%

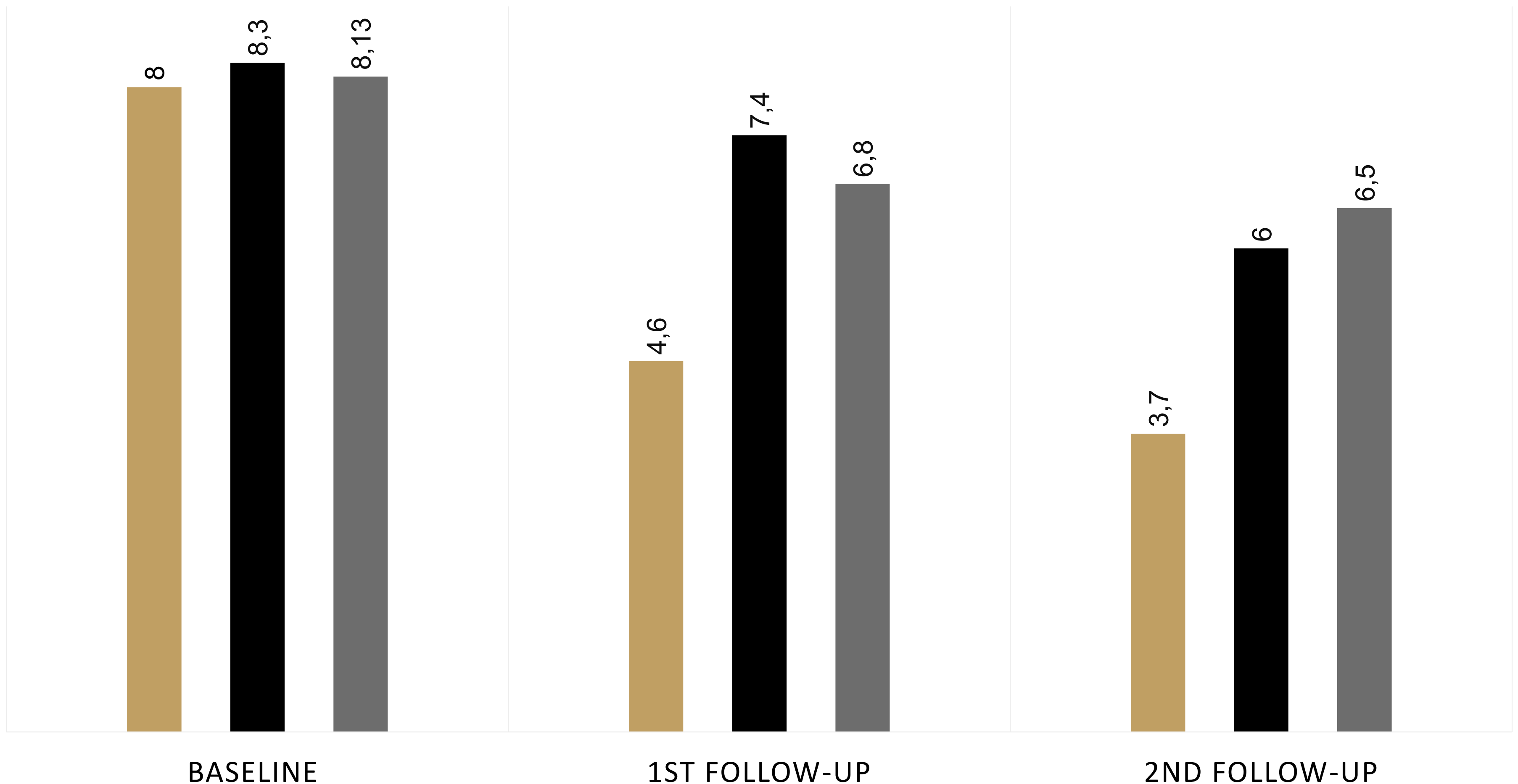
REDUCTION OF PAIN INTENSITY CHANGES IN VAS SCALE

REDUCTION IN VAS SCALE

-53,75% COLLAGEN

-25 % LIDOCAINE

-20,1% SALINE



EVALUATION OF THE SURFACE ELECTROMYOGRAPHY

<i>Pain side</i>	<i>Visit</i>	<i>Group I [μv]</i>	<i>Group II [μv]</i>	<i>Group III [μv]</i>
	<i>Baseline</i>	56.6	59.9	64.1
	<i>1st follow-up visit</i>	32.6	42.4	60.2
	<i>2nd follow-up visit</i>	23.7	36.4	55.2
	<i>EMG changes</i>	-32.9	-23.5	-8.9
	<i>Percentage EMG changes</i>	-59.2%	-39.3%	-14%

<i>No pain side</i>	<i>Visit</i>	<i>Group I [μv]</i>	<i>Group II [μv]</i>	<i>Group III [μv]</i>
	<i>Baseline</i>	34,3	38,7	36,6
	<i>1st follow-up visit</i>	34,6	39,2	34
	<i>2nd follow-up visit</i>	35,2	37,7	36,5
	<i>EMG reduction</i>	+0,9	-1	-0,1
	<i>Percentage EMG reduction</i>	+2,6%	-2,5%	-0,3%

sEMG

MASSETER MUSCLE
ACTIVITY WAS ASSESSED AND
COMPARED WITH
ASYMPTOMATIC SIDE
THERE WERE NO
STATISTICALLY SIGNIFICANT
CHANGES IN SEMG ACTIVITY
ON THE ASYMPTOMATIC
SIDE

Table 6: Reductions in EMG mean values in Group I, Group II, Group III after 14 days

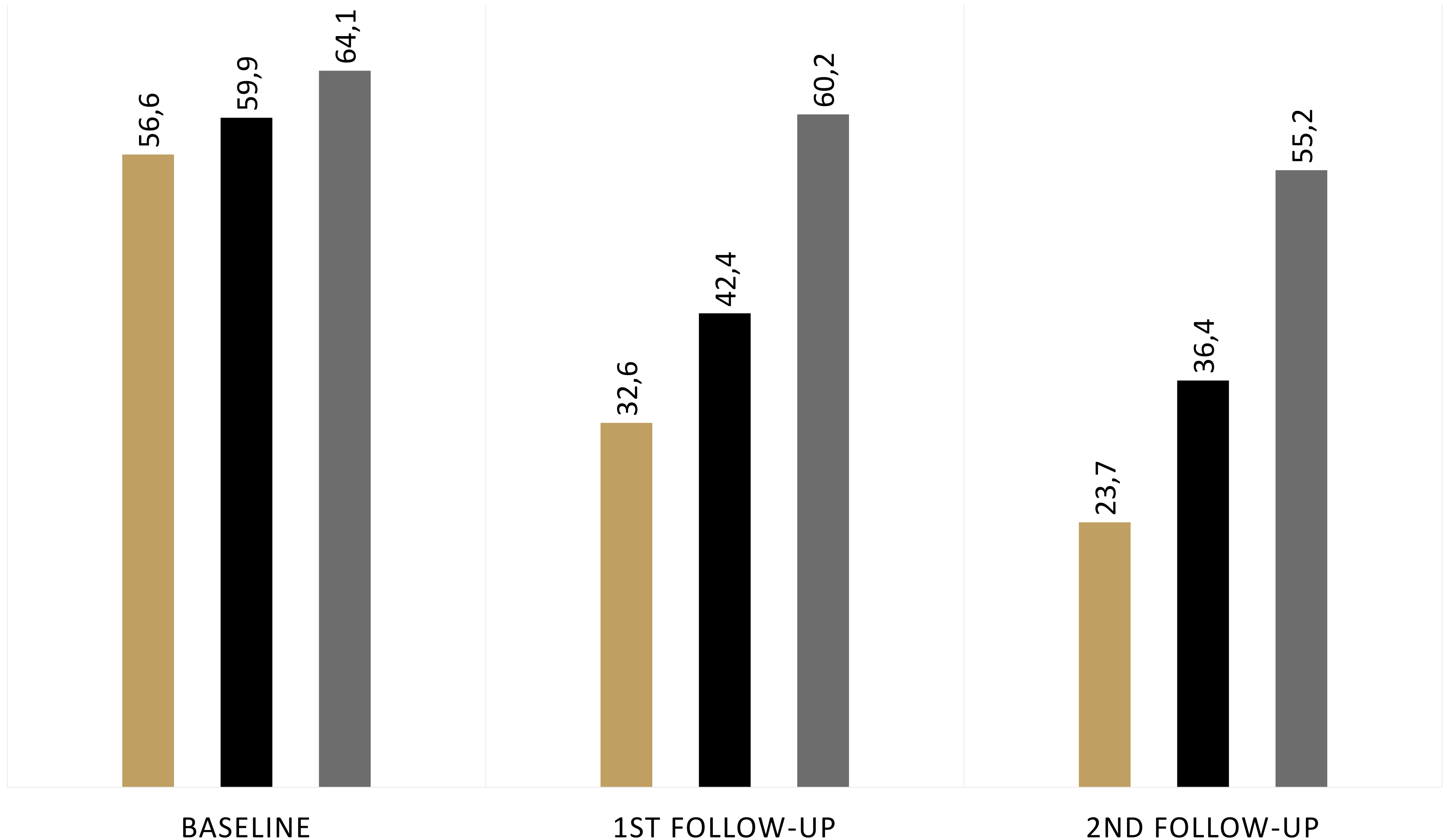
PAINFUL SIDE

REDUCTION IN sEMG [μ V]

59,2% COLLAGEN

39,3 % LIDOCAINE

29% SALINE



EVALUATION OF THE SURFACE ELECTROMYOGRAPHY

<i>Pain side</i>	<i>Visit</i>	<i>Group I [μv]</i>	<i>Group II [μv]</i>	<i>Group III [μv]</i>
	<i>Baseline</i>	56.6	59.9	64.1
	<i>1st follow-up visit</i>	32.6	42.4	60.2
	<i>2nd follow-up visit</i>	23.7	36.4	55.2
	<i>EMG changes</i>	-32.9	-23.5	-8.9
	<i>Percentage EMG changes</i>	-59.2%	-39.3%	-14%
<i>No pain side</i>	<i>Visit</i>	<i>Group I [μv]</i>	<i>Group II [μv]</i>	<i>Group III [μv]</i>
	<i>Baseline</i>	34,3	38,7	36,6
	<i>1st follow-up visit</i>	34,6	39,2	34
	<i>2nd follow-up visit</i>	35,2	37,7	36,5
	<i>EMG reduction</i>		-1	-0,1
	<i>Percentage EMG reduction</i>	+2,6%	-2,5%	-0,3%

sEMG

IN EACH GROUP A STATISTICALLY SIGNIFICANT REDUCTION IN SEMG ACTIVITY WAS OBSERVED
p<0.001

Table 6: Reductions in EMG mean values in Group I, Group II, Group III after 14 days

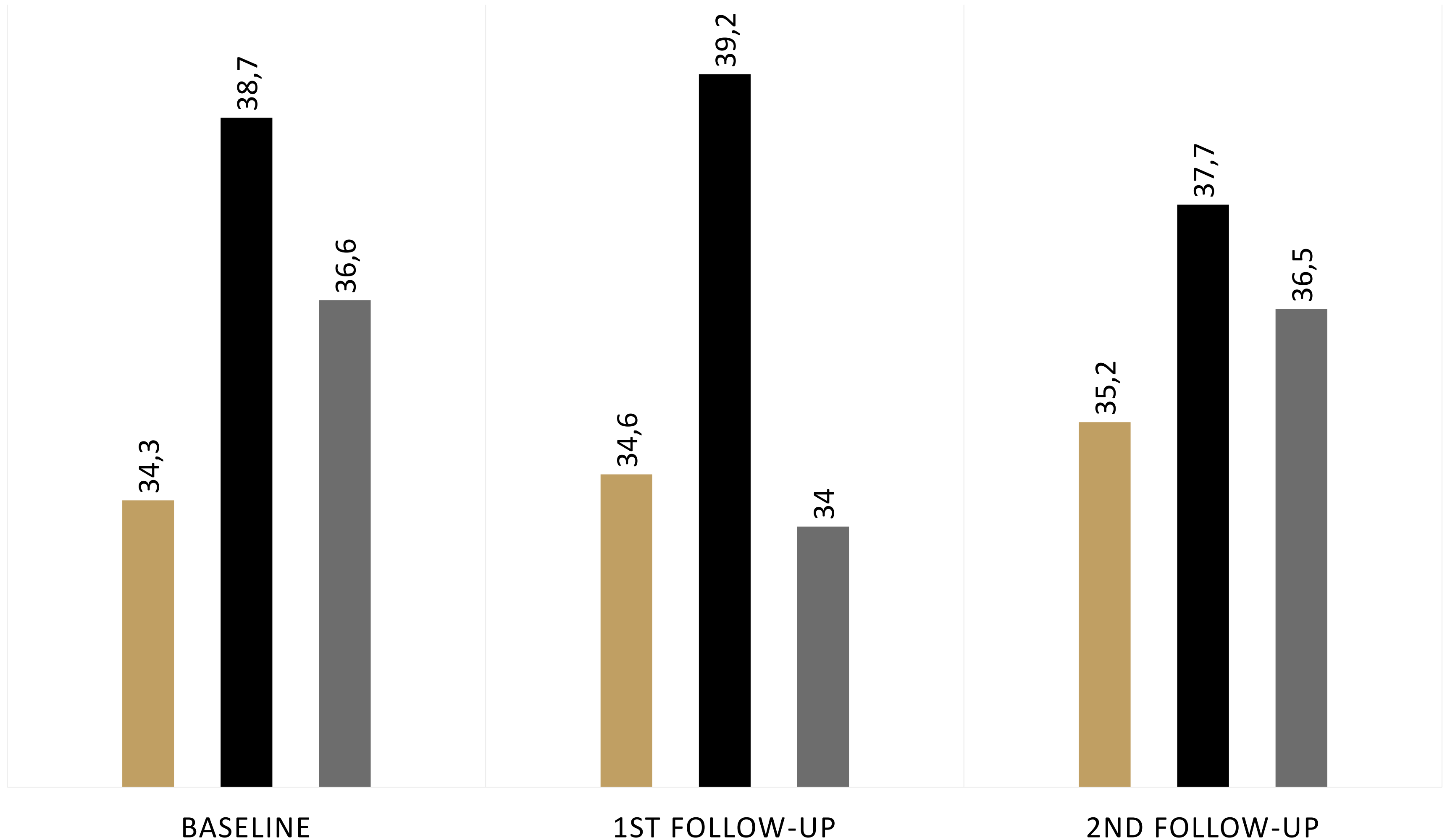
SIDE WITH NO PAIN

REDUCTION IN s EMG [μ V]

+2,6% COLLAGEN

-2,5 % LIDOCAINE

-0,3% SALINE



ADVERSE EFFECTS

PAIN DURING MOVEMENT(30 MIN) AFTER THE INJECTION

EDEMA

MUSCLE STIFFNESS

BRUISES IN THE MASSETER MUSCLE REGION

TEMPORARY ADVERSE EFFECTS

COMPLETELY REVERSIBLE ADVERSE EFFECTS

CONCLUSION

**INTRAMUSCULAR INJECTION OF COLLAGEN IS AN EFFECTIVE
METHOD OF REDUCING MYOFASCIAL PAIN AND sEMG
ACTIVITY IN MASSETER MUSCLES IN TMD PATIENTS**

TRIAL LIMITATIONS

TRIAL LIMITATIONS: SHORT PERIOD OF OBSERVATION,
SINGLE-BLIND NATURE OF THE TRIAL

THANK YOU

**THANK YOU FOR
YOUR ATTENTION**

ATTENTION

LOCATION

Department of Temporomandibular Disorders,
Unit SMDZ in Zabrze,
Medical University of Silesia in Katowice,
2 Traugutta sq, 41-800 Zabrze, Poland

CONTACT US

aleksandra.nitecka@sum.edu.pl
0048 601899069

