**Results of a preclinical study to monitor the effect of SOMA.S in patients with wet AMD**

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**Summary:**

**Purpose: The** aim of the study was to test the effect of the SOMA.S device in patients with wet age-related macular degeneration (AMD). The SOMA.S device works on the principle of controlled release of energy from minerals. The study was commissioned by Somavedic Technologies s.r.o., the manufacturer of the device.

**Methods:** patients with newly diagnosed wet AMD and active CNV in whom anti-VEGF therapy was indicated were included in the study. The following parameters were monitored: best corrected visual acuity (BCVA) on ETDRS optotypes, central macular thickness (CRT), 6x6 mm macular volume (TMV) and OCT angiography. In addition, laboratory blood tests were performed. Patients were given a SOMA.S device to take home and were instructed on how to hook it up at home. A follow-up examination was performed after one month. The study was randomized, double-blind, prospective. Half of the devices did not have a functioning core. After follow-up, patients were assigned to group A, which had a functional SOMA.S device, and control group B, which had only the same-looking lamp.

**RESULTS: A** total of 18 patients completed the study, 9 in each group, 7 women and 2 men in both groups. The mean age was 76.2 years in group A and 75.7 years in group B. The NKZO was 55.3 ± 15.4 and 60.2 ± 13.8 ETDRS letters in group A with a functional device at baseline and after one month, respectively (difference +4.2 ± 6.3 letters). In control group B, the NKZO was 53.7 ± 12.7 at baseline and 53.7 ± 7.5 (difference 0 ± 9.1) ETDRS letters at one month. CRT in group A was 359.6 ± 81.5 μm at baseline and 352.0 ± 99.8 μm (difference -7.6 ± 63.5 μm) after one month. CRT in group B was 441.3 ± 205.6 μm at baseline and 516.3 ± 288.8 μm at one month (difference +75 ± 100.0 μm). TMV in group A was 8.978 ± 0.560 $mm^3$ at baseline and 8.746 ± 0.605 $mm^3$ after one month (difference - 0.232 ± 0.525 $mm^3$ ). TMV in group B was 10.05 ± 2.307 $mm^3$ at baseline and 10.803 ± 3.600 $mm^3$ at one month (difference + 0.757 ± 1.384 $mm^3$ ).

**Discussion:** HFMD is a progressive disease, patients in group A had on average better results after one month than patients in group B. In the group using the active SOMA.S device, the progression of VPMD slowed down during the one-month follow-up.

**CONCLUSION: The** preclinical study demonstrated a positive effect of SOMA.S on slowing the progression of age-related degeneration in the participating patients.

**Introduction:**

The aim of the study was to verify the effect of the SOMA.S device in patients with the wet form of age-related macular degeneration (AMD). The study was conducted at the Eye Clinic of the Faculty of Health Studies of Jan Evangelista Purkyně University in Ústí nad Labem and the Regional Health, a.s. - Masaryk Hospital in Ústí nad Labem, o.z. between 2020 and 2023.

AMD is a disease of the centre of the sharpest vision of the retina and has two forms. The dry form is characterized by a gradual deterioration of central visual acuity due to abnormalities of the retinal pigment epithelium and the gradual development of geographic (map-like) atrophy. The wet form of AMD causes a sudden deterioration of vision due to the formation of the chorioid (choroidal) membrane and leakage of fluid into the retina or into the space under the retina [1].

The moist form occurs in about 10% of all AMD but causes 90% of cases of practical blindness due to AMD [2]. A review of the production data of the General Health Insurance Company of the Czech Republic shows that 10,269 unique insured patients were treated in the diagnostic group Ophthalmology, which includes treatment of chorioid membranes caused by VPMD, as well as a small percentage of chorioid membranes due to rare causes, between January and September 2023. For the same period in 2022, the number of patients was 8,854. The year-on-year increase for the first 9 months of 2022 and 2023 alone is 1,415 patients with chorioid membranes (mostly caused by HPAI) and this is only from the perspective of the largest health insurer in our country [3]. This is therefore a major health and societal problem.

AMD is a multifactorial disease in which genetic and environmental factors are involved. The disease has a very strong age-related association and its prevalence and incidence increases significantly with increasing age. The primary risk factors for the disease include smoking, uncorrected hypertension, atherosclerosis, cataract surgery, and family history of the disease. Other possible risk factors include diabetes mellitus, light

the color of the iris. [4]. Although many risk factors are known, the pathogenesis of the disease remains unclear. However, oxidative stress, inflammation and endothelial dysfunction probably play the most important role, as in other chronic diseases [5]. Tumor

Necrotizing factor alpha (TNFα) is the main cytokine involved in the inflammatory response [6]. A review paper by King et al. investigated the effect of nutrition on VMPD and reported that the main cause of VPMD is oxidative stress, defined as an excess of oxygen free radicals. A balance between antioxidants and free oxygen radicals is therefore essential. Research suggests an important role for antioxidants and other nutrients in reducing the risk of developing AMD [7].

The use of artificial intelligence in the evaluation of biomarkers to predict the progression of AMD is currently being investigated [8].

The treatment of wet AMD is currently performed by intraocular application of anti-vascular endothelial growth factor (anti-VEGF) antibodies; their efficacy has been proven by many studies [9] and especially by clinical practice. In the Czech Republic, the drugs ranibizumab, aflibercept, brolucizumab and faricimab are approved for this treatment.

This study investigated the possibility of improving the wet form of AMD by reducing oxidative stress in

patients using the SOMA.S device during the preparation of planned standard anti-VEGF therapy. The SOMA.S device works on the principle of controlled release of energy from minerals. Somavedic devices (one of which is the SOMA.S) eliminate unwanted excess free radicals during sleep and structure water [10].

The study was commissioned by Somavedic Technologies s.r.o., the manufacturer of the device.

**Methodology:**

Patients with newly diagnosed wet AMD and active CNV in whom anti-VEGF therapy was indicated were included in the study. The study was conducted while patients were awaiting treatment approval and the date of first anti-VEGF injection. Exclusion criteria were the presence of other concomitant macular disease or diabetic retinopathy (DR), untreated arterial hypertension or its decompensation, systemic disease, malignant disease under treatment with chemotherapy or actinotherapy or after such treatment (interval less than 5 years). Arterial hypertension, thyroid disease and diabetes mellitus (DM) without DR symptoms were monitored.

The following parameters were investigated: best corrected visual acuity (BCVA) on ETDRS optotypes, central macular thickness (CRT), macular volume of 6x6 mm (TMV) and OCT angiography. In addition, laboratory blood tests were performed: tumor necrosis factor alpha (TNFα). Blood samples were examined using the TNFα method on an IMMULITE analyzer. Patients were given the SOMA.S machine and instructed how to hook it up at home. A follow-up examination was performed after one month. The study was randomized, double-blind, prospective. Half of the devices did not have a functioning core. After follow-up, patients were assigned to group A, which had a functional SOMA.S device, and control group B, which had only the same-looking lamp.

The statistical analysis was to compare two groups of patients. Due to their small number, the corresponding test was performed in a non-parametric form, i.e. as Mann-Whitney

test. The null hypothesis assumes that the distributions in both groups are identical. Thus, if the resulting p-value is less than 0.05, a statistically significant difference between the two groups is demonstrated at the 5% significance level. Next, a paired Wilcoxon test was performed, comparing the starting and ending median. The tests were performed using FW R-project.

**File:**

A total of 18 patients completed the study, 9 in each group, with 7 women and 2 men in both groups. The mean age was 76.2 ± 10 years, m = 65 (min. 61 and max. 95 years) in group A and 75.7 ± 43.5 years, m = 75 (min. 70 and max. 84 years) in group B. The age of the patients in both groups was statistically compared and no statistically significant difference was found (p = 0.860). However, there was somewhat higher variability in group A.

In group A, CNV was occult in 3 eyes, mixed in 3 eyes (2 of which were at least classic), and classic in 3 eyes. In group B, CNV was occult in 5 eyes, mixed in 3 eyes and classic in 1 eye.

In group A, 7 patients were treated for arterial hypertension, 1 for reduced thyroid function on replacement, and 5 for DM treated with oral antidiabetics. In group B, 7 patients were treated for arterial hypertension, 1 for reduced thyroid function on replacement and no patient for DM.

**Results:**

NKZO was 55.3 ± 15.4 and 60.2 ± 13.8 ETDRS letters in group A with functional device at baseline and after one month (difference +4.2 ± 6.3 letters). In control group B, the NKZO was 53.7 ± 12.7 at baseline and 53.7 ± 7.5 (difference 0 ± 9.1) ETDRS letters at one month (table 1, graphs
1 a 2).

The Mann-Whitney test of the difference in the magnitude of the observed change in NKZO between the two groups was not statistically significant (p=0.329). The Wilcoxon test showed a statistically significant improvement (increase) in NKZO values after one month in group A (p=0.037), while in group B the change was not statistically significant (two-tailed test: p=0.767, improvement: p=0.384).

The change in NKZO after one month in group A was a worsening of 5 or more letters in 1 patient, a change of less than 5 letters in 3 patients, and an improvement of 5 or more letters in 5 patients (Figure 3). The change in NKZO after one month in group B was a worsening of 5 or more letters in 5 patients and an improvement of 5 or more letters in 4 patients (Figure 4).

| **NKZO** (ETDRS letters) | **Group A** | | | **Group B** | | |
|---|---|---|---|---|---|---|
| | **Beginning** | **After a month** | **The Difference** | **Beginning** | **After a month** | **The Difference** |
| **Average** | 55,3 | 60,2 | **4,9** | 53,7 | 53,7 | **0** |
| SD | 15,4 | 13,8 | 6,3 | 12,7 | 7,5 | 9,1 |
| Median | 60 | 63 | **5** | 50 | 55 | **-5** |
| Min | 20 | 25 | -5 | 33 | 43 | -14 |
| Max. | 70 | 75 | 15 | 74 | 65 | 11 |

Table 1: NKZO values in ETDRS letters in both groups

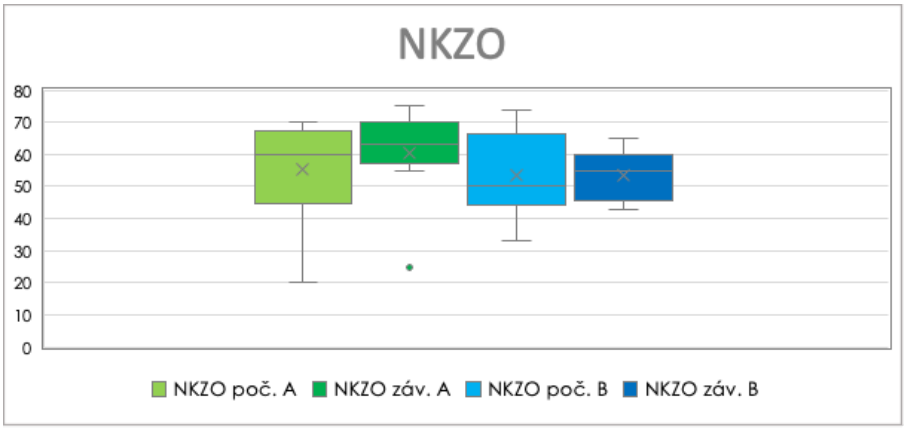



Figure 1. Box plot of NKZO in ETDRS letters in both groups

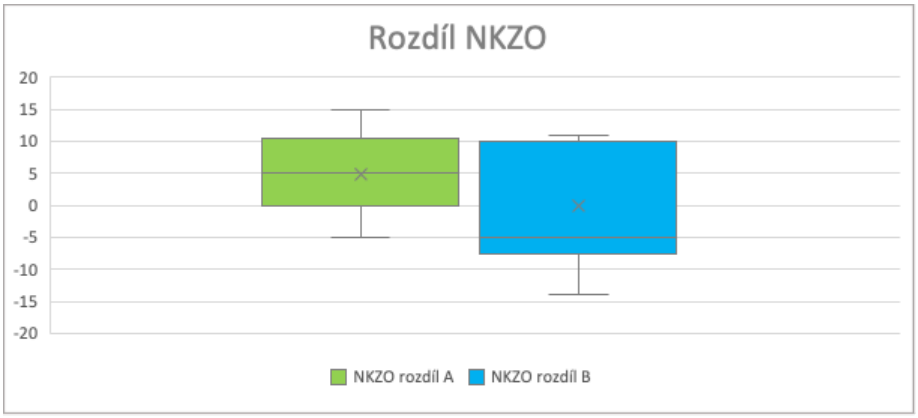
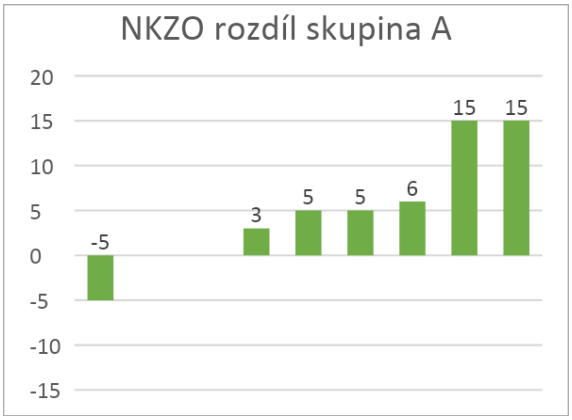
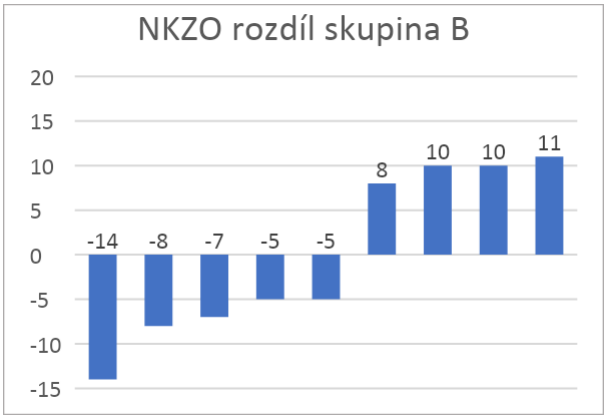



Figure 2: Difference in NCDs by month in ETDRS letters in both groups




Figures 3 and 4: Difference in NPCS after one month compared to baseline NPCS for each eye in ETDRS letters in group A (Figure 3) and group B (Figure 4)

CRT in group A was 359.6 ± 81.5 µm at baseline and 352.0 ± 99.8 µm at one month (difference -7.6

± 63,5 µm). CRT in group B was 441.3 ± 205.6 µm at baseline and 516.3 ± 288.8 µm after one month.

μm (difference +75 ± 100.0 μm) (Table 2, Figures 5 and 6). The Mann-Whitney test of the difference in the magnitude of the observed change in CRT was statistically significant (p=0.022). The Wilcoxon test showed that there was no statistically significant improvement (decrease) in CRT values at one month in group A (p=0.213), but there was a statistically significant worsening (increase) in CRT in group B (p=0.005).

In group A, CRT worsened in 2 eyes and improved in 7 eyes (Figure 7). In group B, all 9 patients experienced worsening CRT (Figure 8).

| **CRT (μm)** | **Group A** | | | **Group B** | | |
|---|---|---|---|---|---|---|
| | **Beginning** | **After a month** | **The Difference** | **Beginning** | **After a month** | **The Difference** |
| **Average** | 359,6 | 352 | **-7,6** | 441,3 | 516,3 | **75** |
| SD | 81,5 | 99,8 | 63,5 | 205,6 | 288,8 | 100,0 |
| Median | 380 | 367 | **-22** | 361 | 385 | **24** |
| Min | 235 | 217 | -109 | 256 | 278 | 17 |
| Max. | 500 | 498 | 136 | 954 | 1259 | 305 |

Table 2: CRT values in μm in both groups

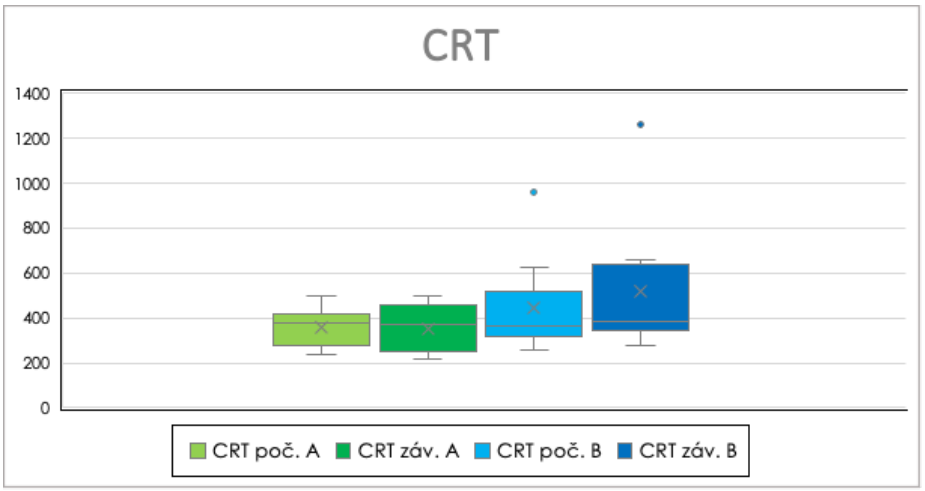



Figure 5. Box plot of CRT in μm in both groups

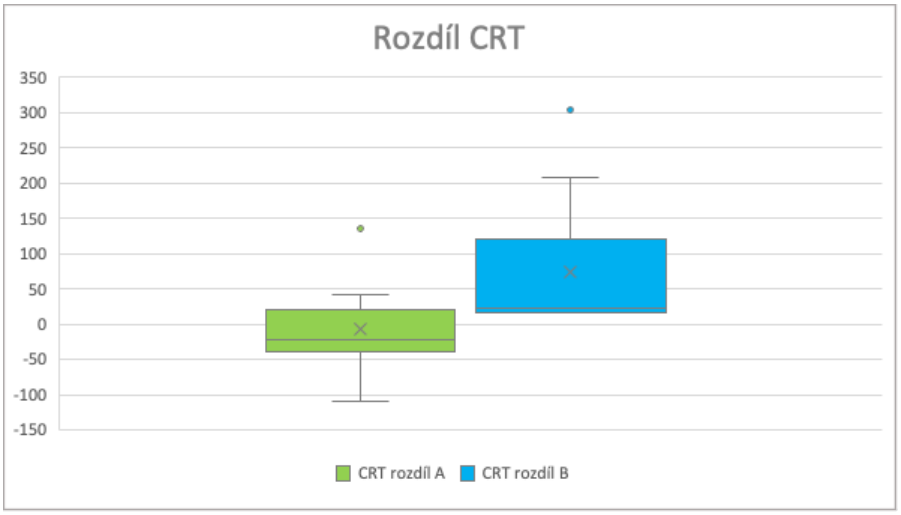
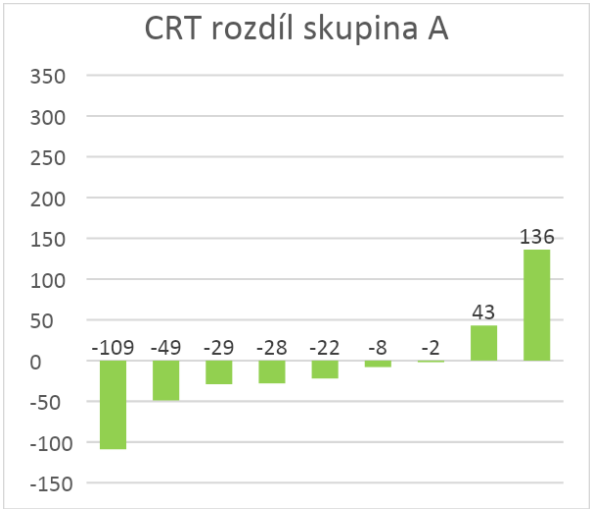
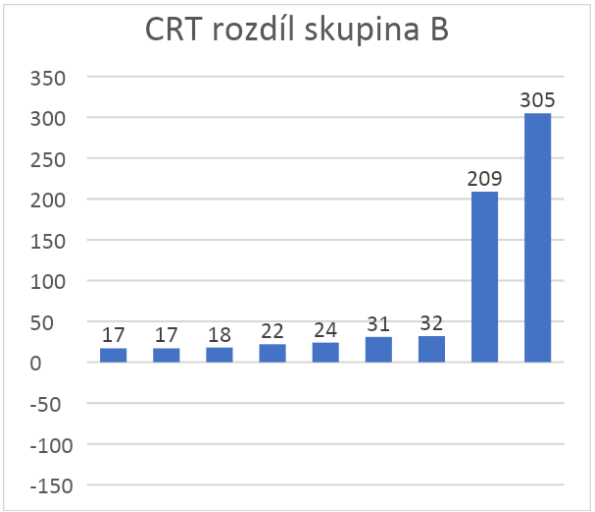



Figure 6: Difference in CRT in µm after one month in both groups



Graphs 7 and 8: Difference in CRT in μm at one month compared to baseline CRT in individual eyes in group A (graph 7) and group B (graph 8)

TMV was 8.978 ± 0.560 $mm^3$ in group A at baseline and 8.746 ± 0.605 $mm^3$ at one month (difference

- 0,232 ± 0,525 $mm^3$ ). TMV in group B was 10.05 ± 2.307 $mm^3$ at baseline and 10.803 ± 3.600 $mm^3$ at one month (difference + 0.757 ± 1.384 $mm^3$ ) (Table 3, Figures 9 and 10). The Mann-Whitney test for the difference in the magnitude of the observed change in TMV between the two groups was not statistically significant (p = 0.094). The Wilcoxon test showed that there was no statistically significant improvement (reduction) in TMV in group A (p = 0.150), and no statistically significant change in group B (two-tailed test: p = 0.203, improvement: p = 0.102).

In group A, TMV worsened in 3 eyes and improved in 6 eyes (Figure 11). In group B, TMV worsened in 6 eyes and improved in 3 eyes (Figure 12).

| **TMV $(mm)^3$** | **Group A** | | | **Group B** | | |
|---|---|---|---|---|---|---|
| | **Beginning** | **After a month** | **The Difference** | **Beginning** | **After a month** | **The Difference** |
| **Average** | 8,978 | 8,746 | **-0,232** | 10,05 | 10,803 | **0,757** |
| SD | 0,560 | 0,605 | 0,525 | 2,307 | 3,600 | 1,384 |
| Median | 8,81 | 8,6 | **-0,1** | 9,19 | 8,92 | **0,1** |
| Min | 8,28 | 7,85 | -1,54 | 8,15 | 8,22 | -0,51 |
| Max. | 9,84 | 9,74 | 0,42 | 15,9 | 19,93 | 4,03 |

Table 3. TMV values in $mm^3$ in both groups

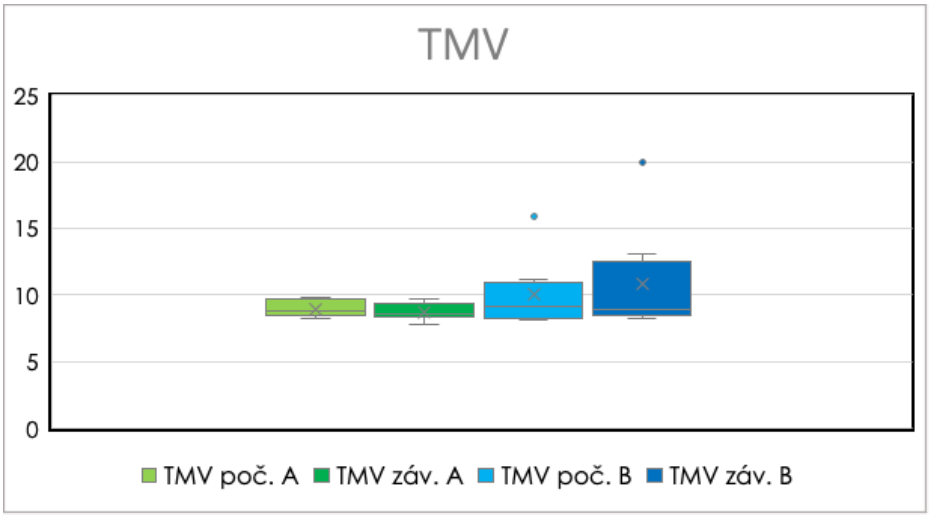



Figure 9. Box plot of TMV in $mm^3$ in both groups

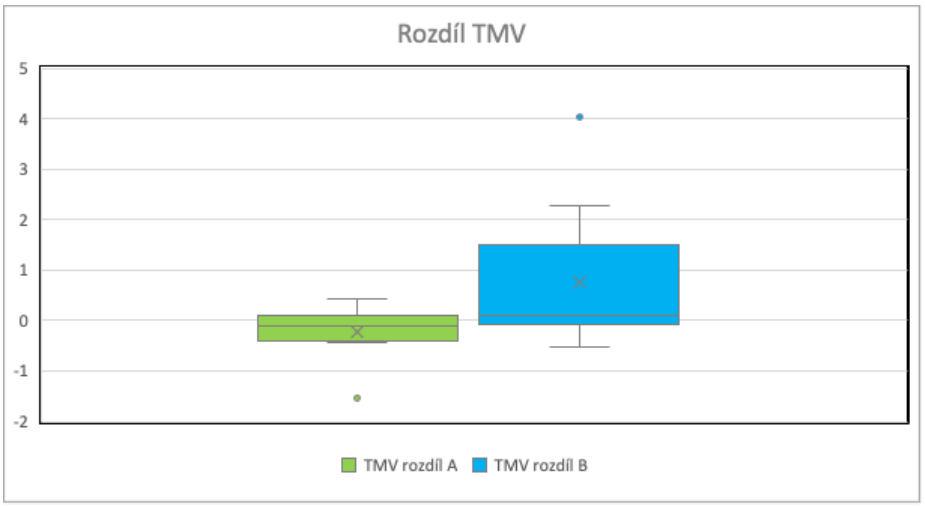
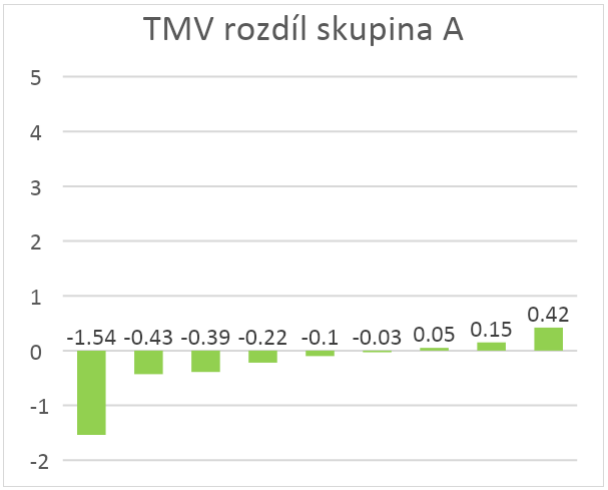
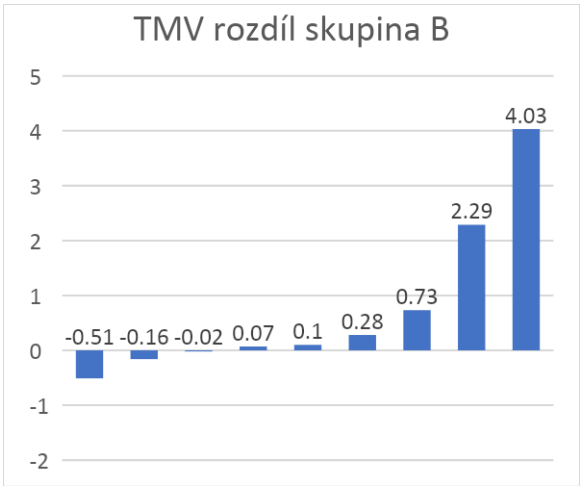



Figure 10: Difference in TMV in $mm^3$ by month in both groups




Figures 11. and 12. Difference of TMV in $mm^3$ after one month compared to baseline TMV in individual eyes in group A (graph 11) and group B (graph 12)

TNFα in group A was 8.456 ± 2.479 pg/ml at baseline and 8.340 ± 2.526 pg/ml after one month (difference - 0.116 ± 1.494 pg/ml). TNFα in group B was 9.858 ± 4.359 pg/ml at baseline and 10.111 ± 3.915 pg/ml after one month (difference + 0.253 ± 0.988 pg/ml) (Table 4, Figures 13 and 14). The Mann-Whitney test of the difference in the magnitude of the observed change in TNFα between the two groups was not statistically significant (p = 0.724). The Wilcoxon test showed that there was no statistically significant improvement (decrease) in TNFα in group A (p = 0.571), and the increase in TNFα in group B was also not statistically significant (p = 0.180).

In group A, TNFα worsened in 3 patients and improved in 6 patients (Figure 15). In group B, TNFα worsened in 6 patients and improved in 3 patients (Figure 16).

| TNFα (pg/ml) | Group A | Group B |
|---|---|---|

| | Beginning | After a month | The Difference | Beginning | After a month | The Difference |
|---|---|---|---|---|---|---|
| **Average** | 8,456 | 8,340 | **-0,116** | 9,858 | 10,111 | **0,253** |
| SD | 2,479 | 2,526 | 1,494 | 4,349 | 3,915 | 0,988 |
| Median | 8,9 | 8,13 | **-0,46** | 7,54 | 8,43 | **0,89** |
| Min | 4,89 | 4,72 | -1,8 | 5,33 | 6,51 | -1,89 |
| Max. | 12,0 | 12,2 | 1,92 | 20,6 | 20,2 | 1,21 |

Table 4: TNFα levels in pg/ml in both groups

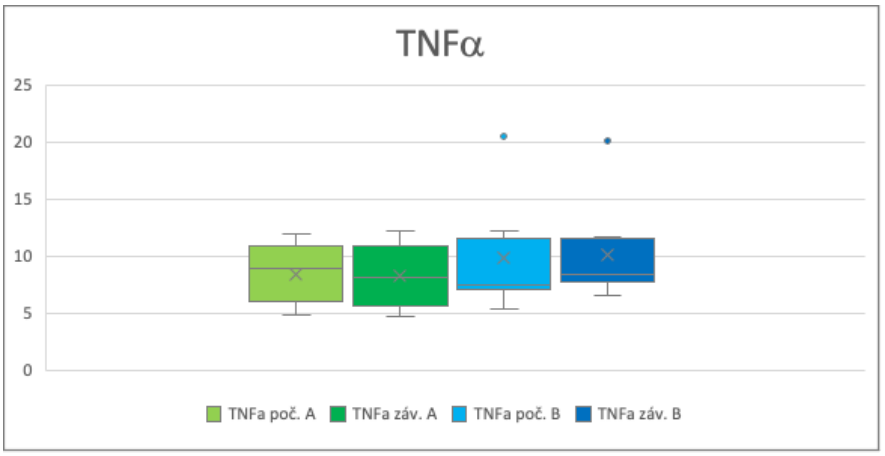



Figure 13. Box plot of TNFα in pg/ml in both groups

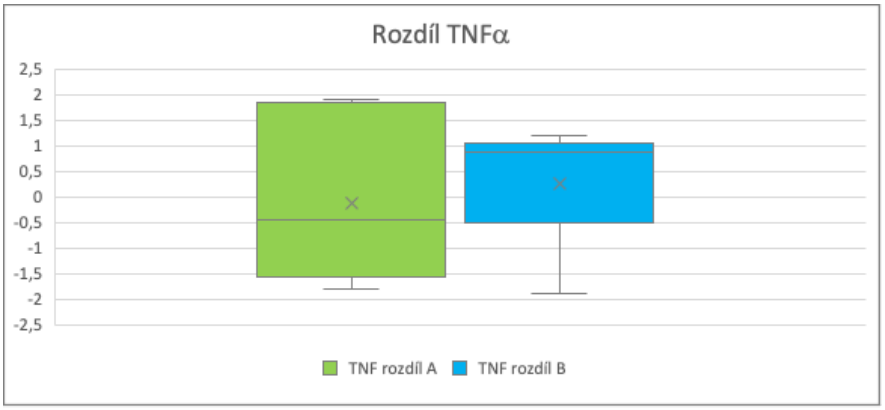
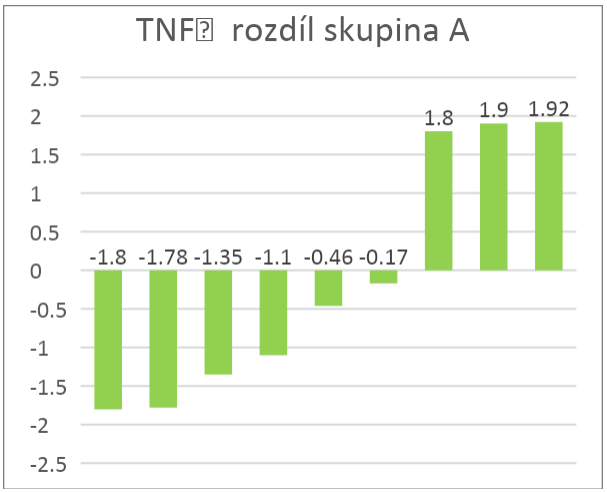



Figure 14: Difference in TNFα in pg/ml after one month in both groups



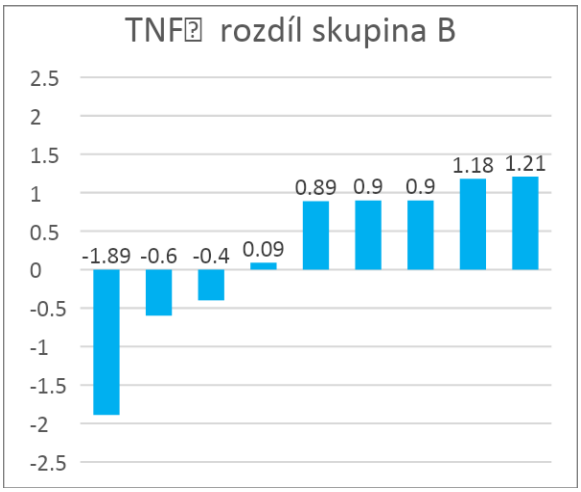




Figure 15 and 16. Difference in TNFα in pg/ml after one month compared to baseline TMV in individual eyes in group A (Figure 15) and group B (Figure 16)

**Discussion:**

The duration of the study and the number of participants was affected by repeated waves of the Covid-19 pandemic.

In group A with a functional device, there was an average improvement in NKZO, CRT, TMV and TNFα. In control group B, there was no change in NKZO, but CRT, TMV and TNFα values were on average worsened.

Due to the size of the sample, non-parametric tests were used for statistical evaluation. A statistically significant Mann-Whitney test of the difference in the magnitude of the observed change in CRT was demonstrated at a significance level of $p < 0.05$.

A paired Wilcoxon test comparing the baseline and endpoint median revealed a statistically significant improvement in NKZO in group A (at the $p < 0.05$ significance level) compared with a nonsignificant change in group B. In addition, there was a statistically insignificant change in CRT in group A, compared with a significant worsening of CRT in group B at the $p < 0.01$ significance level. For the remaining variables studied, the change was not statistically significant at the minimum 5% level. Clinically, there was a significant improvement in the level of vision (NKZO) and a slower progression of intraocular findings (CRT and TMV - reduction of retinal edema in the macula) in group A with active SOMA.S devices. In contrast, group B without active devices showed no change in vision (NKZO) and progressive continuation of intraocular changes in terms of increasing retinal edema (CRT and TMV values).

Age-related macular degeneration is a chronic, multifactorial, progressive disease. From this perspective, it is significant that patients in group A had better overall outcomes than those in group B at one month.

The gold standard treatment for the wet form of AMD is anti-VEGF therapy. The disease itself and its treatment are associated with stress and anxiety in patients [11]. There are papers in the literature investigating the effect of dietary, nutritional and lifestyle changes on the development and progression of VPMD [5, 7, 12 - 16]. Our work demonstrates another important factor that can be part of the treatment strategy for HPAI, which is the improvement of the patient's living environment.

**Conclusion:**

A preclinical study has demonstrated a positive effect of SOMA.S-induced changes in the environment and water structure on slowing the progression of age-related macular degeneration in participating patients.

**Quote:**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