

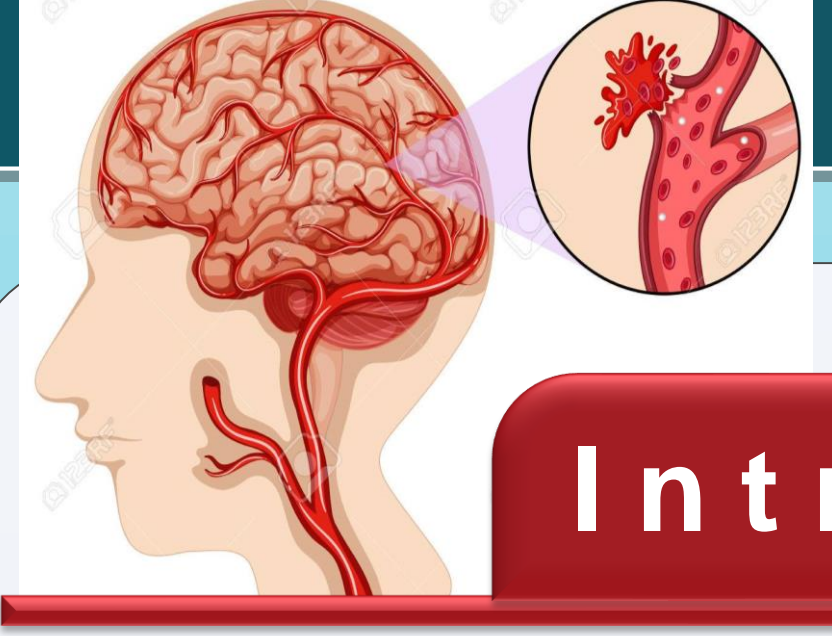


# Advanced 3D modeling for prediction and quantification of the perihematomal brain edema formation after ICH: implications of biochemical, radiological and clinical variables



Vladimir Rendevski<sup>1</sup>, Boris Aleksovski<sup>2</sup>, Ana Mihajlovska Rendevska<sup>3</sup>

<sup>1</sup>University Clinic of Neurosurgery, Medical Faculty, "Ss. Cyril and Methodius" University, Skopje, Republic of North Macedonia  
<sup>2</sup>Faculty of Natural Sciences and Mathematics, "Ss. Cyril and Methodius" University, Skopje, Republic of North Macedonia  
<sup>3</sup>University Clinic of Radiology, Medical Faculty, "Ss. Cyril and Methodius" University, Skopje, Republic of North Macedonia



## Introduction

**ICH as a global problem...**  
 the least treatable, deadliest and most devastating subtype of all strokes

**Estimated 30-day case fatality...**  
 40.4%

**Among survivors...**  
 induces the worst long-term neurological outcome of all strokes

severe disability and usually life-long major functional dependence among patients

The worst neurological deterioration after ICH occurs due to the formation of...  
**perihematomal brain edema**

mass effect, increased ICP, herniation  
 Significant risk factor for **poor prognosis** and increased in-hospital mortality

The identification of the **main risk factors** which directly or indirectly drive the brain edema formation is particularly challenging, allowing **prediction of the brain edema formation** on the basis of initial variables.  
 Implication in clinical decision making!

What is known from the scientific work till now...  
 Some literature findings...

## Methods

### Study design

#### Prospective, longitudinal cohort study

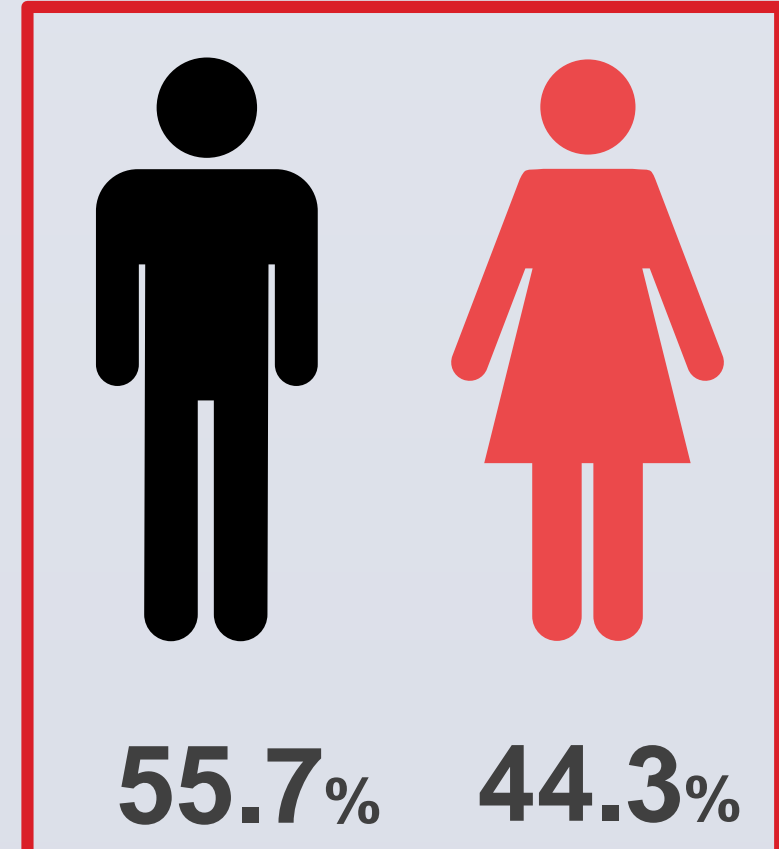
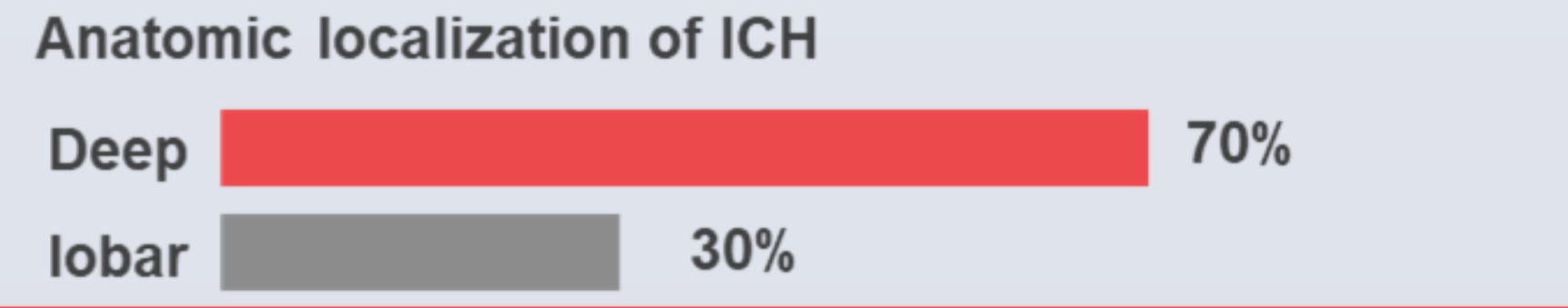
**Cohort group:** conservatively-treated patients with acute, primary, supratentorial intracerebral hemorrhage, without severely altered state of consciousness at admission (unarousable unresponsiveness, coma) and, without severe complications during the hospitalization process (as intraventricular and subarachnoid bleeding or hematoma expansion which require surgical intervention)

**Treatment:** hospitalization within the first 24h from the symptom onset at the University clinic of Neurology and Neurosurgery, Skopje; **same treatment initiation in all patients** with osmolar, anti-hypertensive, neuroprotective and symptomatic therapy in compliance with the present evidence-based management strategies

**Period of investigation:** 01.1.2014 – 30.8.2018

**Total number of subjects included in the study:** 70

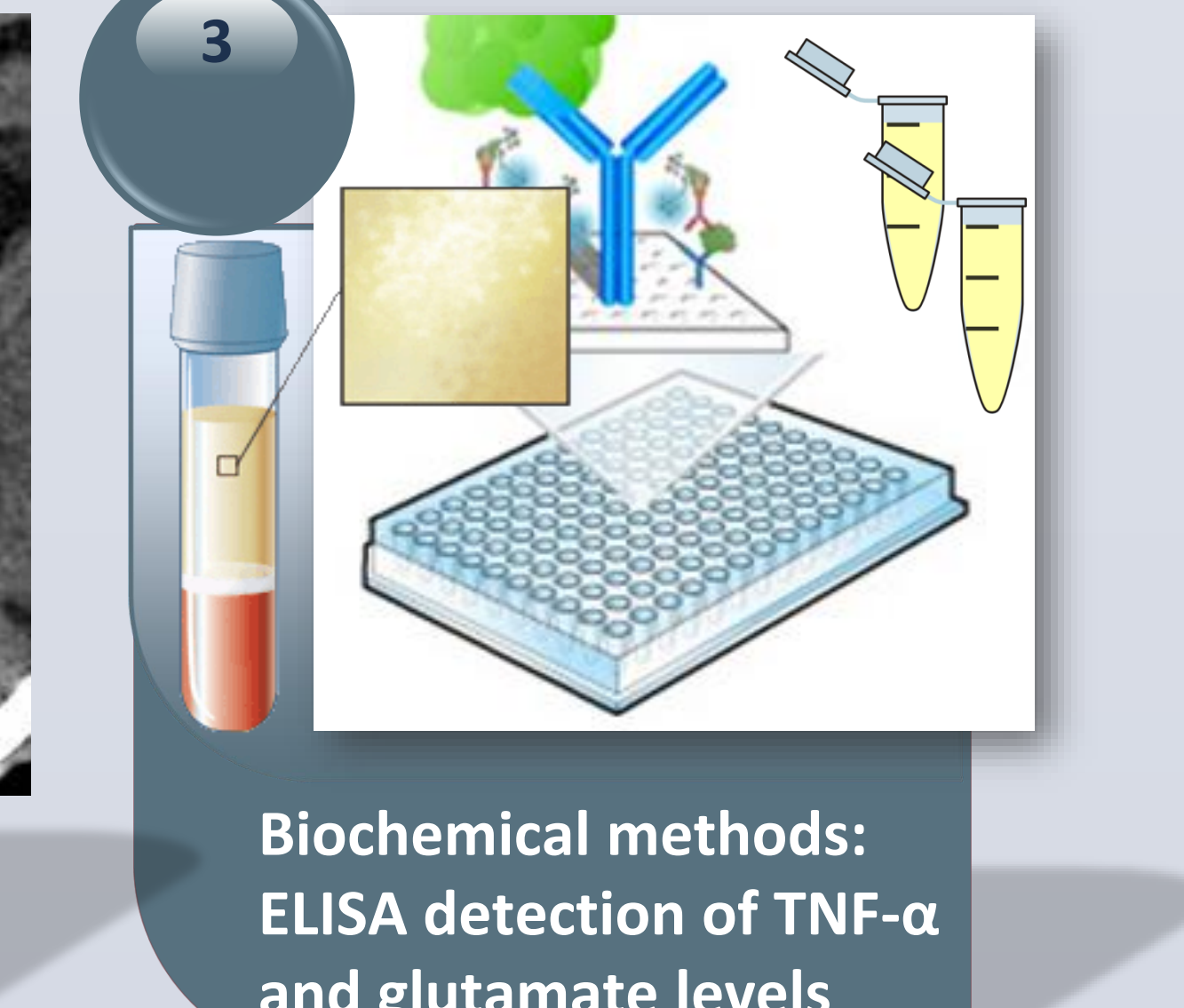
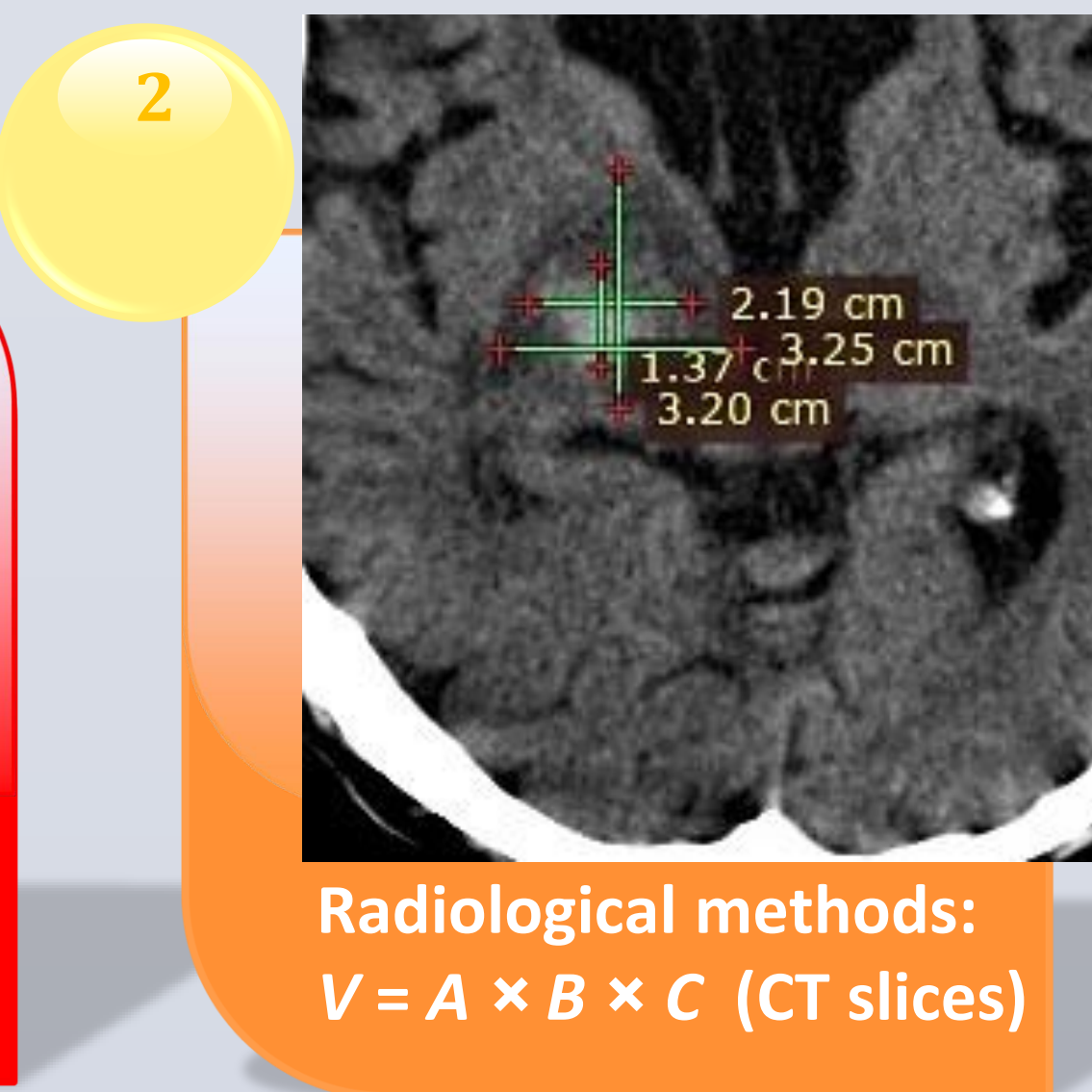
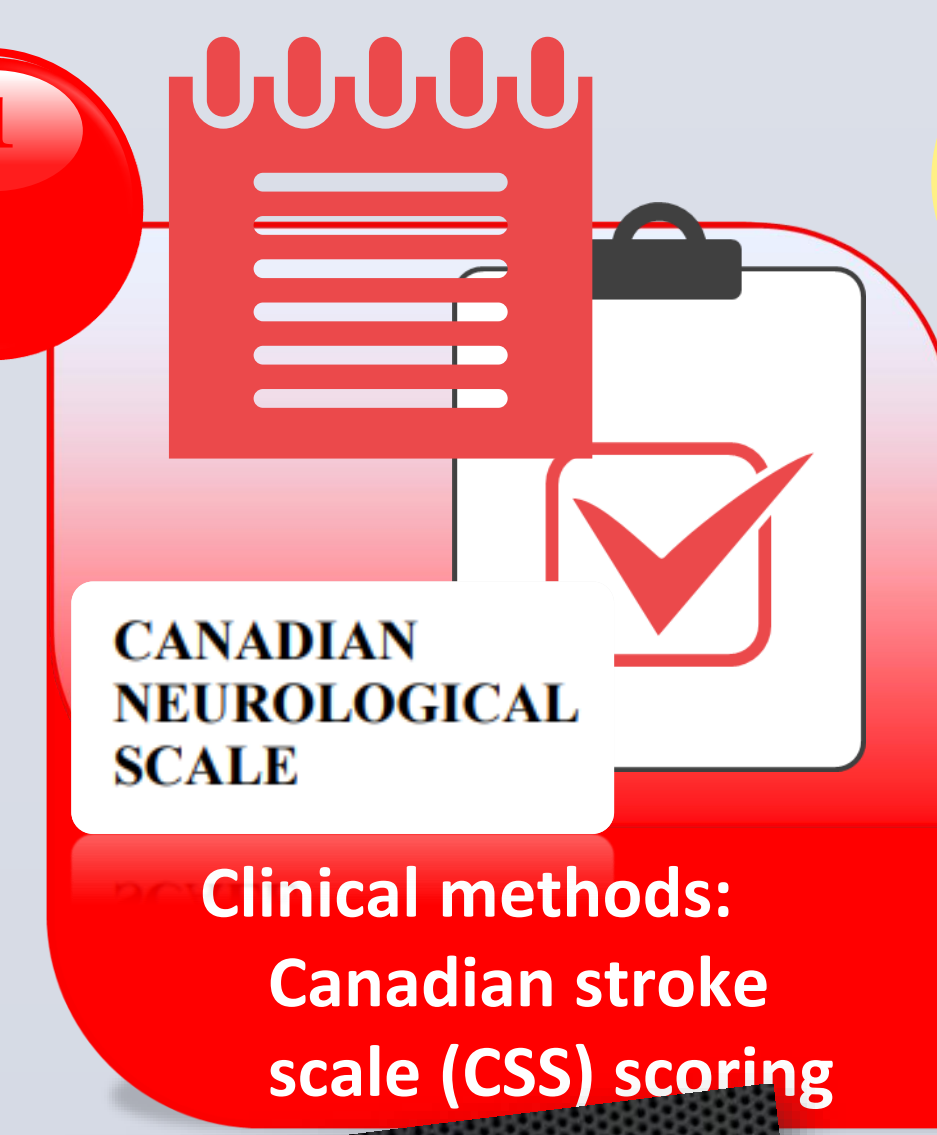
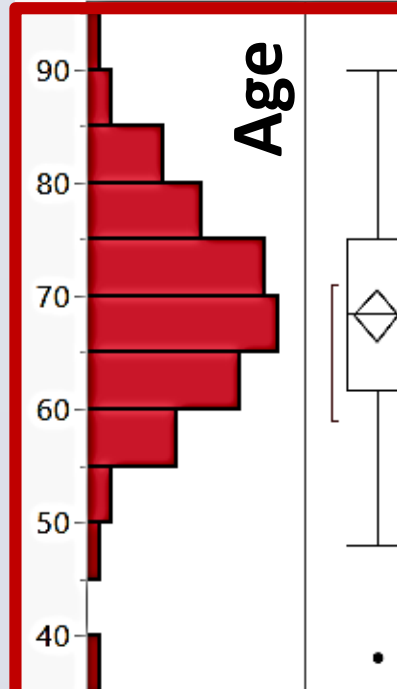
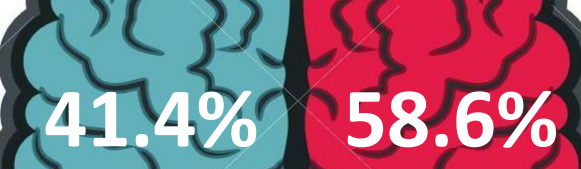
### Basic characteristics



### Diabetes mellitus



### Hemispheric side



## Results

### Multiple regression Model summary (JMP® 14 Statistical discovery, SAS Ins.)

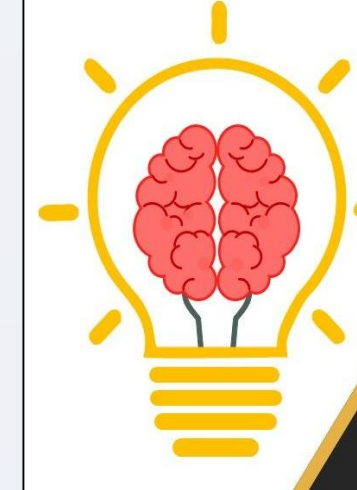
| Variables                                  | B        | t     | p         | LogWorth of the effects | Values | $\beta$ | VIF  |
|--|----------|-------|-----------|-------------------------|--------|---------|------|
| Intercept                                  | -49.4949 | -3.47 | 0.0009**  |                         | /      | 0       | /    |
| Admission TNF- $\alpha$ (pg/mL)            | 0.3292   | 6.95  | 0.00001** |                         | 8.581  | 0.6329  | 2.47 |
| Admission glutamate ( $\mu$ mol/L)         | 0.2484   | 3.04  | 0.0034*   |                         | 2.461  | 0.2146  | 1.48 |
| ICH volume at admission (cm <sup>3</sup> ) | 0.3162   | 2.79  | 0.0070*   |                         | 2.115  | 0.2159  | 1.79 |
| Presence of diabetes mellitus [yes]        | -6.3180  | -2.43 | 0.0179*   |                         | 1.747  | -0.1595 | 1.28 |
| CSS score at admission                     | 1.6299   | 1.50  | 0.1387    |                         | 0.858  | 0.1272  | 2.14 |
| Admission blood glucose (mmol/L)           | 0.9283   | 1.33  | 0.1891    |                         | 0.723  | 0.0838  | 1.19 |
| Anatomic localization of ICH [deep]        | 2.6807   | 0.89  | 0.3777    |                         | 0.423  | 0.0642  | 1.56 |

B – Unstandardized B coefficients; t – t-test statistics value;  $\beta$  – standardized coefficients. \*\*p < 0.001, \*p < 0.05.



**High overall predictive capacity:** 77% of the variation in the volumes of the edema were accounted by the defined seven model effects

$$R^2 = 0.7922, R^2_{Adj} = 0.7687, \text{Root Mean Square Error (RMSE)} = 18.5425$$



### High significance of the model

(One-way ANOVA resume:  $F = 33.7592, **p = 7.4 \cdot 10^{-19}$ )

Without any multicollinearity issues (VIF values less than 2.5)  
 Residuals followed approximately normal distribution

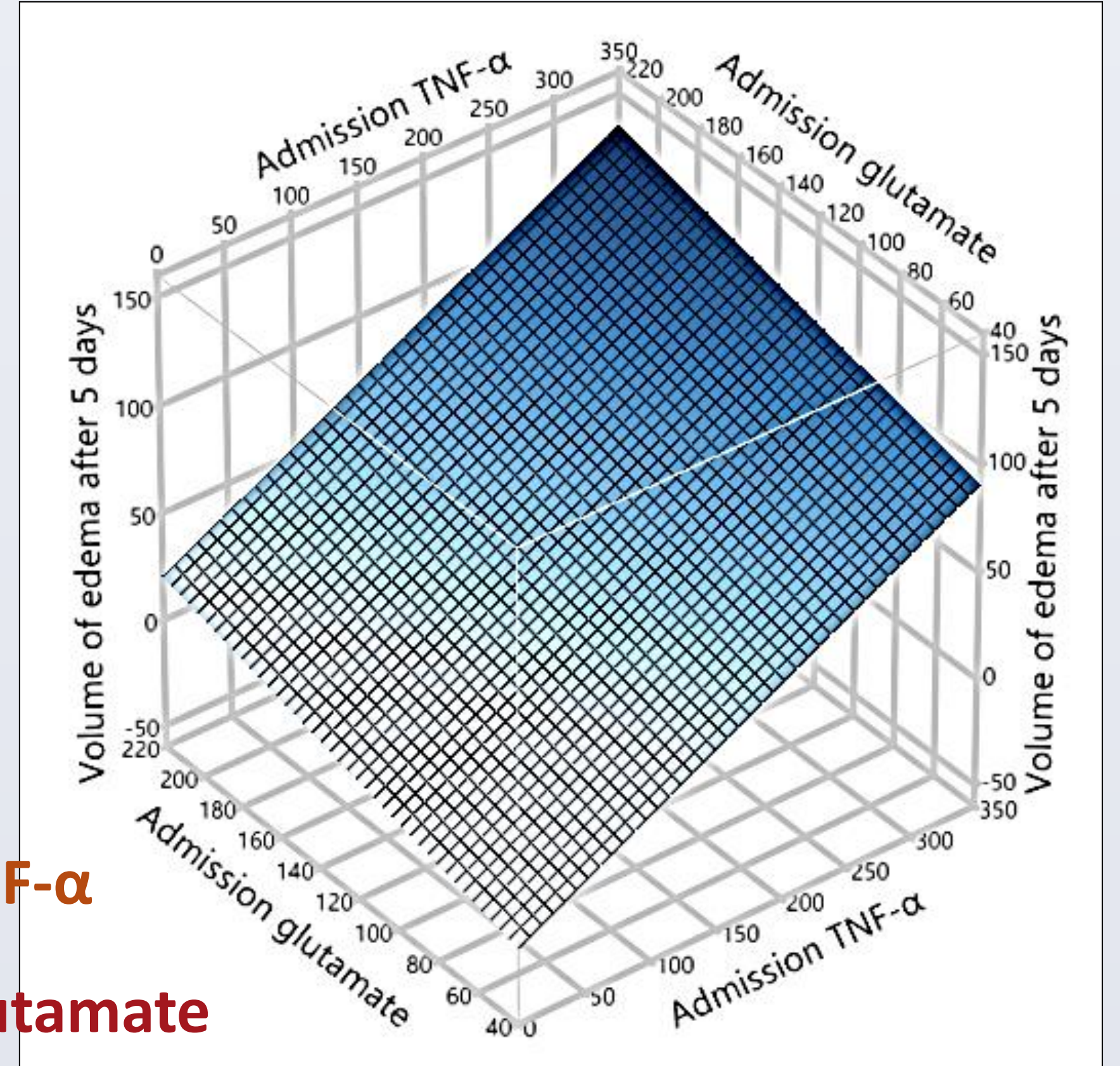
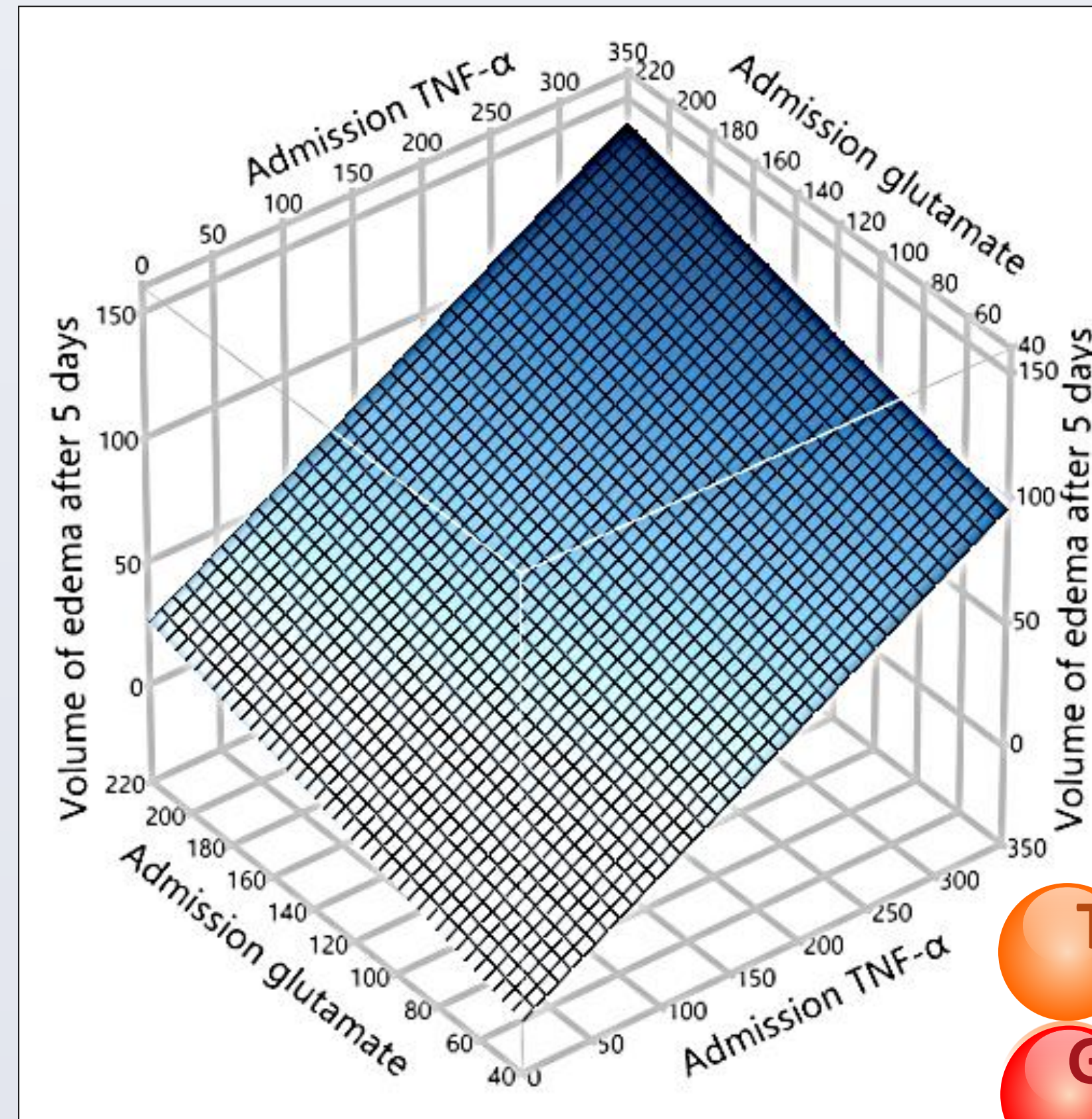
good overall characteristics and fit!

Reliability and validity!

### 3D Modeling, Edema prediction and Interactive plots

$$V_{\text{edema}} = 0.3292 \cdot c_{\text{TNF-}\alpha} + 0.2484 \cdot c_{\text{glutamate}} + 0.3162 \cdot V_{\text{ICH}} + 1.6299 \cdot \text{CSS} + 0.9283 \cdot c_{\text{glucose}} - 49.4949 + a$$

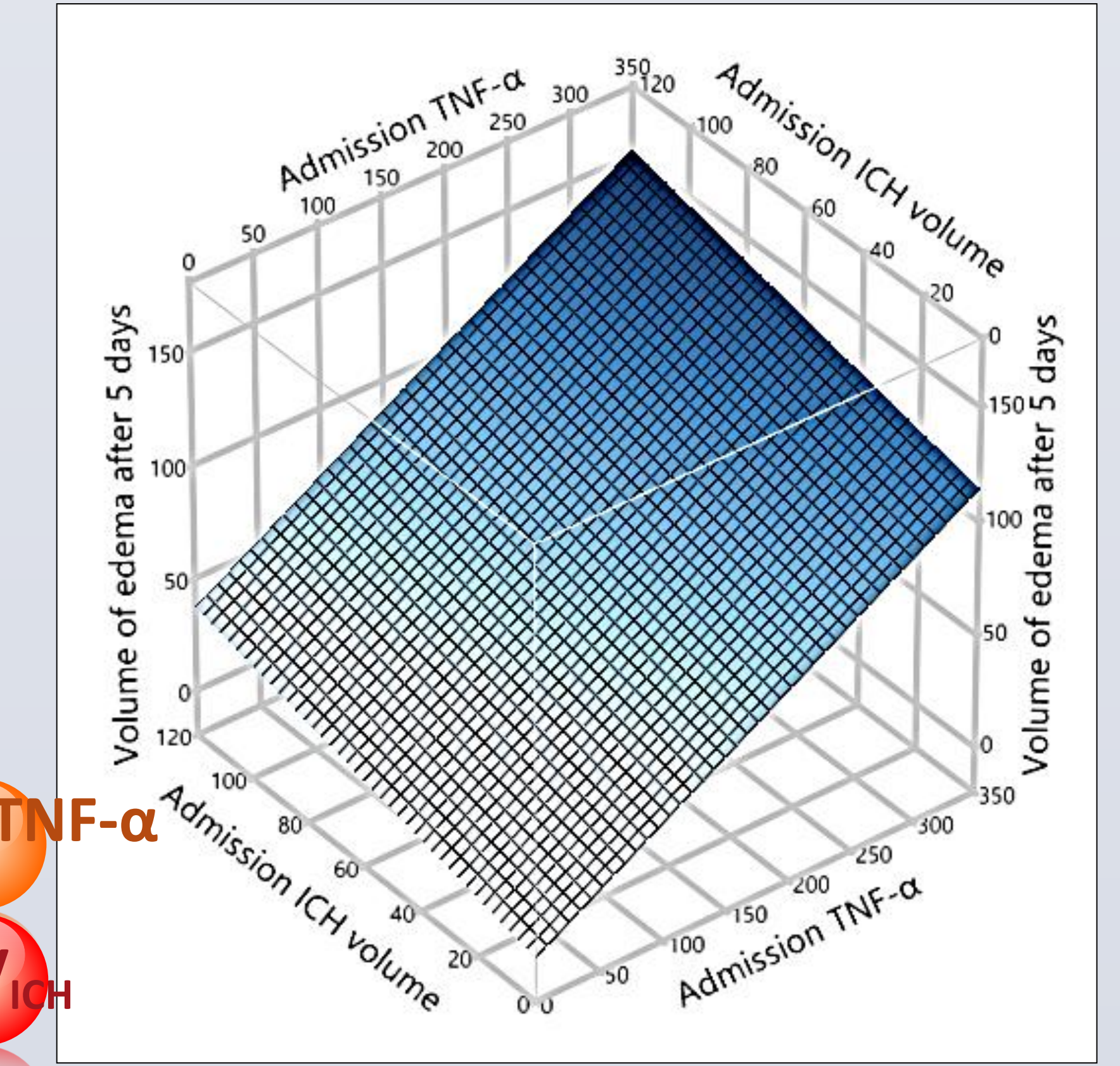
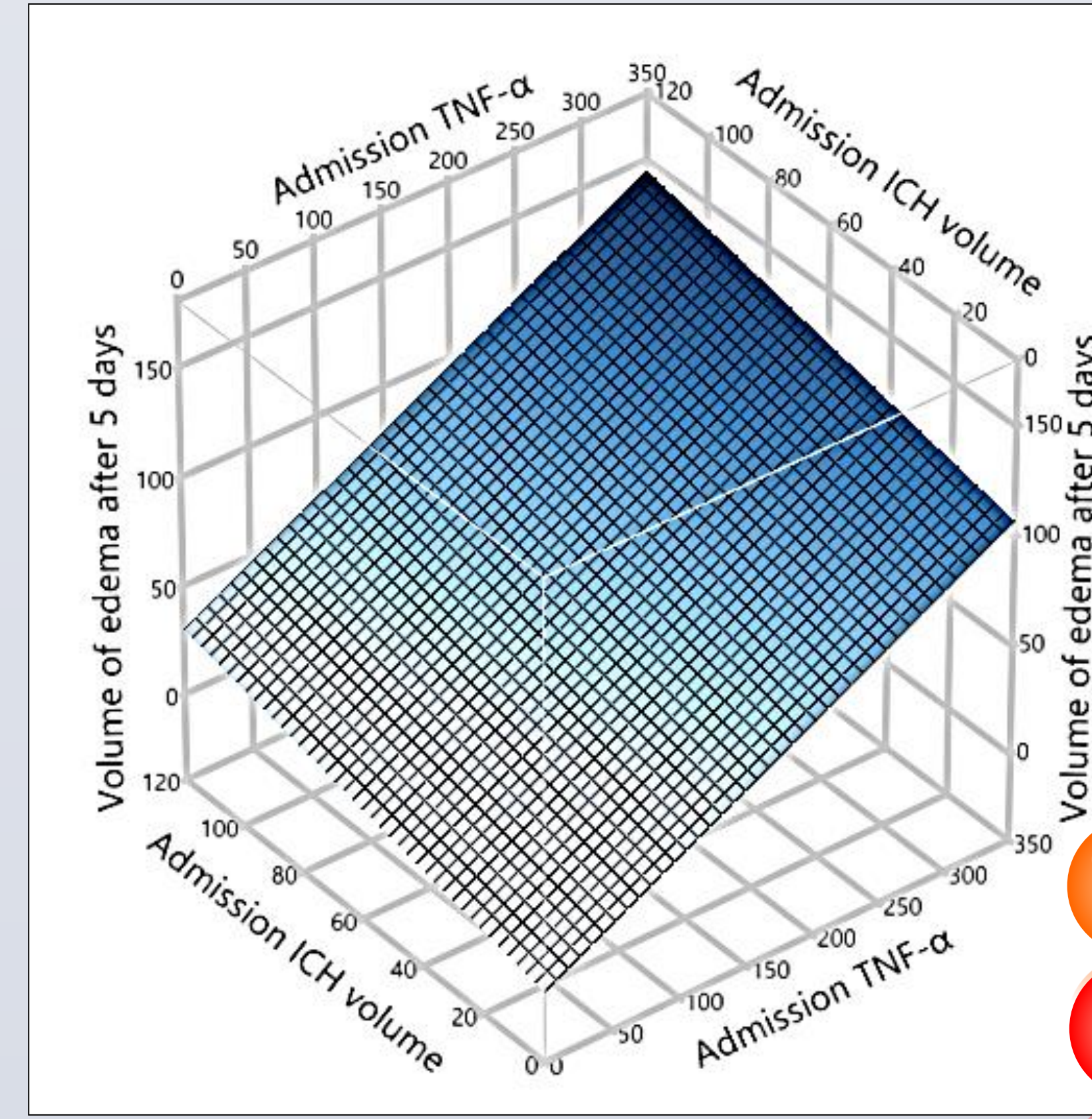
(a summarizes effects of anatomic localization and presence of Diabetes)



### Diabetic patients with deep ICH

### Diabetic patients with lobar ICH

Other predictor values based on their median value from this study (admission glucose 7,6 mmol/L; admission CSS score 7,0; admission ICH volume 18,7)



### Diabetic patients with deep ICH

### Non-diabetic patients with lobar ICH

Other predictor values based on their median value from this study (admission glucose 7,6 mmol/L; admission CSS score 7,0; admission glutamate 108.98  $\mu$ mol/L)

### Development of software app for quantification of the perihematomal edema volume

| Horiz                            | Vert                  | Factor                                  | Current X              |
|----------------------------------|-----------------------|---|------------------------|
| <input type="radio"/>            | <input type="radio"/> | Admission blood glucose (mmol/L)        | 8                      |
| <input type="radio"/>            | <input type="radio"/> | Anatomic localization of ICH            | 0 deep (basal ganglia) |
| <input type="radio"/>            | <input type="radio"/> | Admission CSS score                     | 5                      |
| <input type="radio"/>            | <input type="radio"/> | Admission glutamate ( $\mu$ mol/L)      | 130,95                 |
| <input checked="" type="radio"/> | <input type="radio"/> | Admission TNF- $\alpha$ (pg/mL)         | 162,89                 |
| <input type="radio"/>            | <input type="radio"/> | Admission ICH volume (cm <sup>3</sup> ) | 18                     |
| <input type="radio"/>            | <input type="radio"/> | Presence of diabetes mellitus           | 0 yes                  |

Response: Pred Formula Volume of the perihematomal brain edema after 5 days (cm<sup>3</sup>)

Contour: 70,43 | Current Y: 54,283883 | Lo Limit: | Hi Limit: |

## Conclusions

We believe that the constructed models and the developed interactive plots could be beneficial for clinical decision making between conservative treatment and surgical intervention, especially in the group of threatened ICH patients where high volumes of the edema are expected to occur during the patient's hospitalization trajectory.

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