

ELEM
THE VIRTUAL
HUMANS FACTORY

Clexio
Biosciences



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CASE STUDY

OPTIMIZED DRUG DELIVERY USING ELEMS IN SILICO
MODELING FOR CLEXIO'S CLE-500 DEVICE TO
RELIEVE CLUSTER HEADACHES

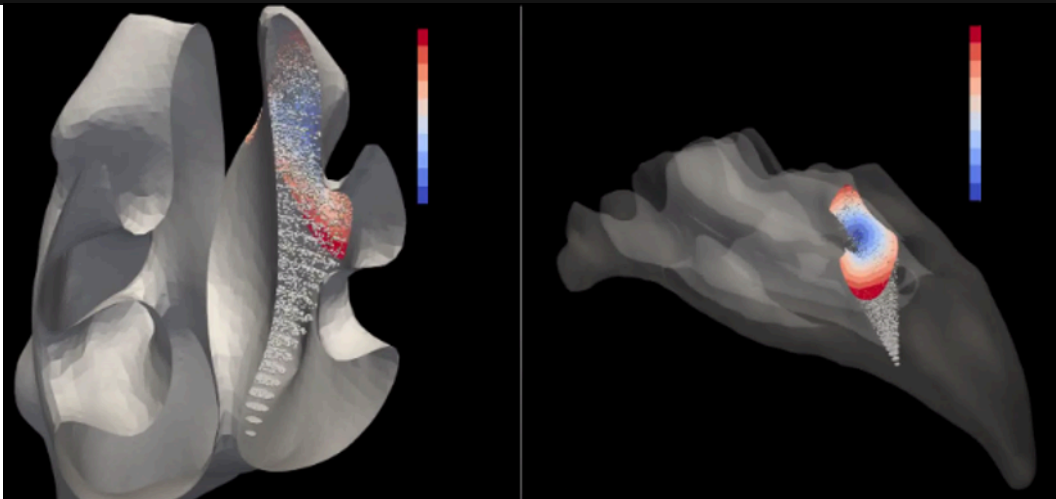


Figure 3: Visualizing the spray plume, deposited particles and distance from the target in the nasal cavity

“ ELEM performed 5,400 discrete experiments on our device in patient-specific scenarios, each simulating the trajectory of thousands of particles deposited. This digital twin approach identified the optimal parameters to maximize population reach and discovered complex cases that would otherwise be hard to imagine, let alone prototype and test in vitro. **This study added great value to developing and optimising our SPRACISE device**, designed to immediately relieve cluster headaches through targeted drug delivery to the sphenopalatine ganglion (SPG).

- **Shai Assia, Head of Medical Development,
Clexio Biosciences**



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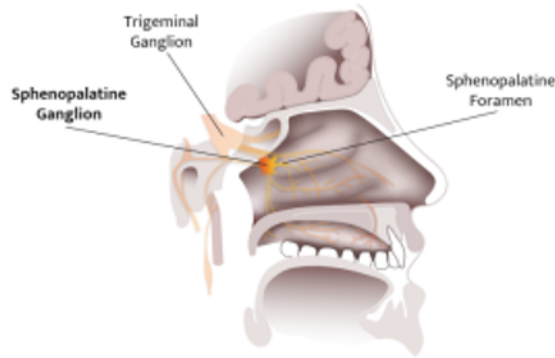


Figure 1: Location of Sphenopalatine Ganglion in the nasal cavity

For over a century, neural modulation of the sphenopalatine ganglion (SPG) has been a subject of study (Sluder G, 1908), employing various techniques with demonstrated efficacy in reducing Cluster Headache pain (CLE-500, 2021).

The SPG, an extracranial parasympathetic nerve ganglion, is intricately linked to Cluster Headache attacks triggered by the trigeminal-autonomic reflex. It's believed to play a significant role in the manifestation of autonomic

symptoms like tearing and nasal congestion. **Clexio Biosciences is at the forefront of developing CLE-500, an innovative intranasal drug-device combination targeting the SPG.** This investigational therapy is designed for immediate relief of cluster headaches, yet it hasn't received commercial approval. The device operates by blocking the nerve pathway associated with the SPG, aiming to alleviate pain within just 15 minutes.

“ In this study, we demonstrate how useful virtual human populations are in enhancing and augmenting the data from real essays. **We produced tangible and realistic results for Clexio** that were directly related to their business. We will be delighted to strengthen our relationship to further advance.

Mariano Vázquez, Chief Scientific Office, ELEM Biotech

ELEMS IN SILICO IMPACT FOR PATIENT-CONTROLLED DRUG-DEVICE CLE-500

A total of **5400 simulations** were carried out. The results were post-processed, creating a dataset that was analyzed to gain insight into optimal parameter combinations for the highest population reach. To achieve this, a pipeline is established from the patient's CT scan to obtain the outcome of drug delivery for **a set of design parameters relating to Clexios patient-controlled drug device CLE-500**. A set of 10 cases are studied using different combinations of α , β , γ and L using the left side of the nasal cavity. **Additional runs were made on the right side of 2 selected cases to check for the pipeline validity.**

QUESTIONS OF INTEREST

- 01** Effect of γ on individual and population level.
- 02** Best performing combination of parameters: α , β , γ , L.
- 03** Effect of L on population reach.

IN SILICO TEST EXECUTION AND METHODOLOGY

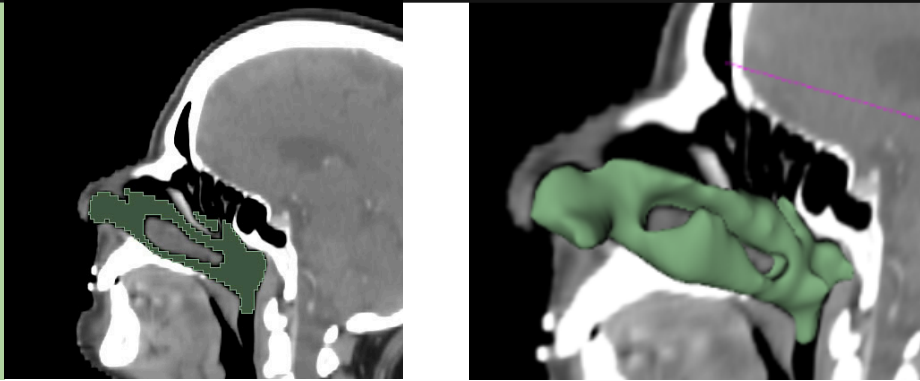
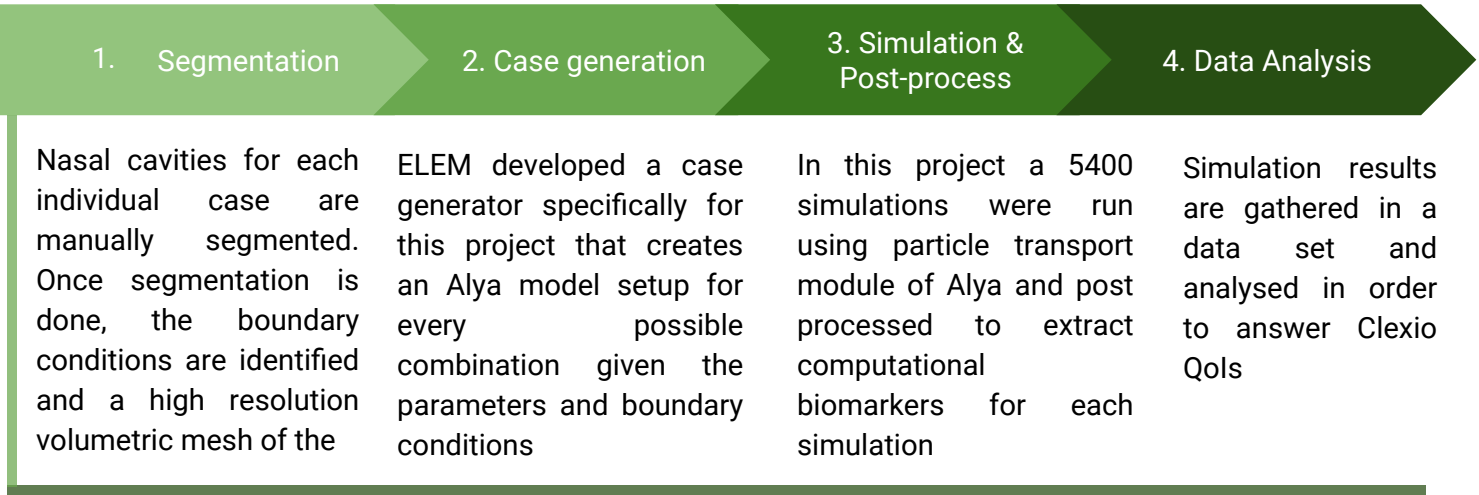
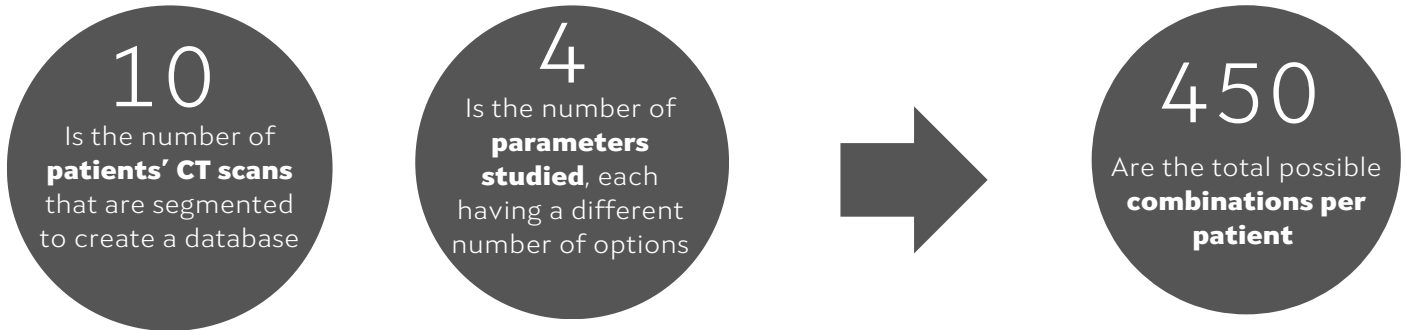


Figure 2: Segmentation of the nasal cavity from a CT scan



1. Segmentation
Nasal cavities for each individual case are manually segmented. Once segmentation is done, the boundary conditions are identified and a high resolution volumetric mesh of the

2. Case generation
ELEM developed a case generator specifically for this project that creates an Alya model setup for every possible combination given the parameters and boundary conditions

3. Simulation & Post-process
In this project a 5400 simulations were run using particle transport module of Alya and post processed to extract computational biomarkers for each simulation

4. Data Analysis
Simulation results are gathered in a data set and analysed in order to answer Clelio Qols

MODEL AND TEST PARAMETERS

Model Input Parameters	Output Computational Biomarkers
<ul style="list-style-type: none"> • α • β • γ • L 	<ul style="list-style-type: none"> • Geodesic mean distance • Percentage of particles within defined ranges of SPG

CONCLUSIONS

ELEM's in silico analysis identified the optimal parameters to work for the highest percentage of the population. This helped guide product development and, thereby, led to optimal product outcomes.

As a result of the process, a pipeline was created, starting with a patient CT scan and finishing with results describing the outcome of deposition for each possible combination of parameters. This pipeline serves as a basis for a study on populations. **ELEM's Virtual Population generator can create synthetic populations on which virtual device trials can be carried out.**

Reference:

CLE-500. (2021). Retrieved from <https://www.clexio.com/pipeline/cle-500/>

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