Laser tissue interactions during Laser Trabeculoplasty using the SOLX Titanium Sapphire laser:

The detailed interaction of the laser beam with the tissue during laser trabeculoplasty and the long-term tissue response are still relatively poorly understood.

The current theory for LT is that laser radiation is selectively absorbed by the melanin pigments in the TM. Collagen and water and most other cellular material are essentially transparent to visible and near-infrared laser radiation. Absorption produces a temperature increase of the melanin granules, which propagates to surrounding tissue by heat diffusion. Laser heating induces thermal damage in the TM by cell death or thermal denaturation. There are currently two main theories to explain the changes in IOP after LT. According to the "mechanical theory", heating induces collagen shrinkage, which in turn increases the intertrabecular spaces and facilitates outflow. According to the "cellular theory", thermally-induced thermal damage induces a wound healing response with formation of new trabecular meshwork cells with increased outflow activity.

The region of tissue surrounding the melanin granules that is heated by diffusion can be estimated by the heat diffusion length, a parameter which depends on the laser pulse duration and on the thermal properties of the tissue. Using the thermal properties of water as a model, the diffusion length, in mm, is $0.47t_p^{1/2}$, where t_p is the pulse duration.

An equally important parameter affecting laser-tissue interaction is the depth of penetration of photons in the TM. The penetration depth determines how deep into the TM the laser energy is deposited. Lasers emitting at wavelengths that are strongly absorbed will not penetrate as deep in the TM. The penetration depth is quantified by the absorption coefficient, in units of cm^{-1}. The absorption coefficient is the inverse of the average depth of penetration of photons in the tissue.

An optical-thermal model is required to predict the temperature distribution in the TM during LT. A typical optical thermal for laser-tissue interaction consists of two steps: first it predicts the light distribution in the irradiated tissue, and second it calculates the resulting temperature distribution. The light distribution can be predicted using a light propagation model, such as Monte-Carlo simulations or the diffusion approximation. The temperature distribution in the tissue is usually calculated by solving the bio-heat equation.

Developing an accurate model for LT is difficult for several reasons. First the TM is a heterogeneous tissue where light is selectively absorbed by pigmented cells, and there is no good model for the density of pigmented cells and its variations in the TM. Second, the optical and thermal properties of the TM and of the pigmented cells have not been well characterized.

As part of the SOLX Phase I project, we developed a preliminary qualitative optical-thermal model of LT to be able to predict and compare the effects of various lasers on the TM during LT. The model will be refined in Phase II and III of the project to provide a quantitative estimation of the laser effects.

The preliminary optical model of the trabecular meshwork is shown in figure 1. The optical model assumes that the TM is a multilayer structure, with layers of water, pigmented cells, and collagen. Each layer is assumed to be homogeneous. This model simulates the anatomical structure of the TM, which consists of several layers of collagenous trabecular beams separated by intertrabecular spaces filled with aqueous. In the TM, the cells are wrapped around the trabecular beams.

The model assumes that a laser beam propagating in the TM will be selectively absorbed in the pigmented cell layers. Absorption of laser radiation will induce a temperature increase that will initially be localized in the irradiated areas of the pigmented cell layers. During irradiation, heat will slowly diffuse from the melanin granules to surrounding areas of the TM.

This simplified preliminary model can be used to qualitatively compare the effects of ALT, SLT and SOLX LT. Note that the values of the penetration depths used below are only rough estimates calculated assuming a 1% pigment per volume concentration of melanin. These values are used mainly to provide a comparison of the penetration depth at the different wavelengths.

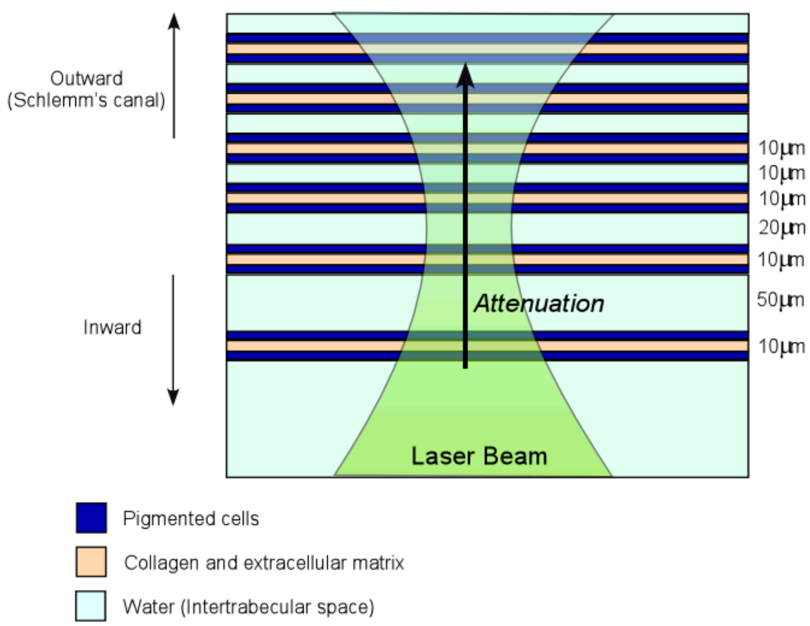

Figure 1: Optical model for laser beam propagation in the trabecular meshwork.

In ALT, the pulse duration is 0.1s, which corresponds to a diffusion length of 300 µm. The estimated penetration depth in the TM at 514nm is 45µm. Heat will therefore be initially deposited in the first few pigmented layers of the TM, but will diffuse well beyond the initial zone of heat deposition during irradiation (Figure 2).

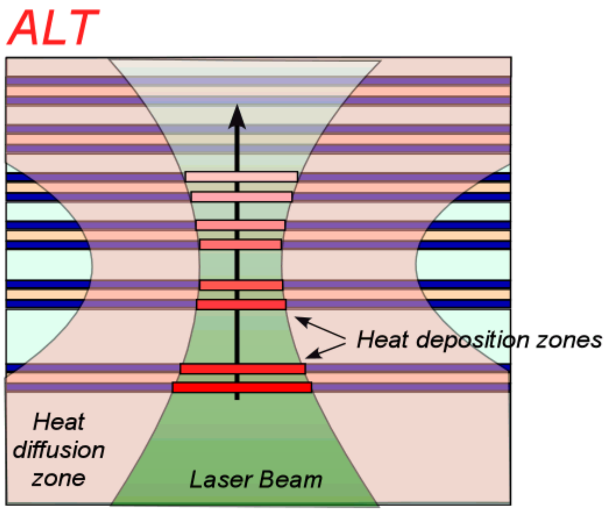

Figure 2: Predicted effect of ALT. The regions in bright red show the initial deposition of heat in the pigmented cell layers, before diffusion. The region in light red shows the total heated area at the end of the laser pulse due to heat diffusion.

In SLT, the pulse duration is 3ns, which corresponds to a diffusion length of 0.05 µm. The estimated penetration depth in the TM at 532nm is 50µm. Heat will therefore be initially deposited in the first few pigmented layers of the TM at a depth comparable to ALT. However, during SLT, heat deposition will remain localized to the pigments within the cell, since the predicted diffusion length is well below 1 µm (Figure 3).

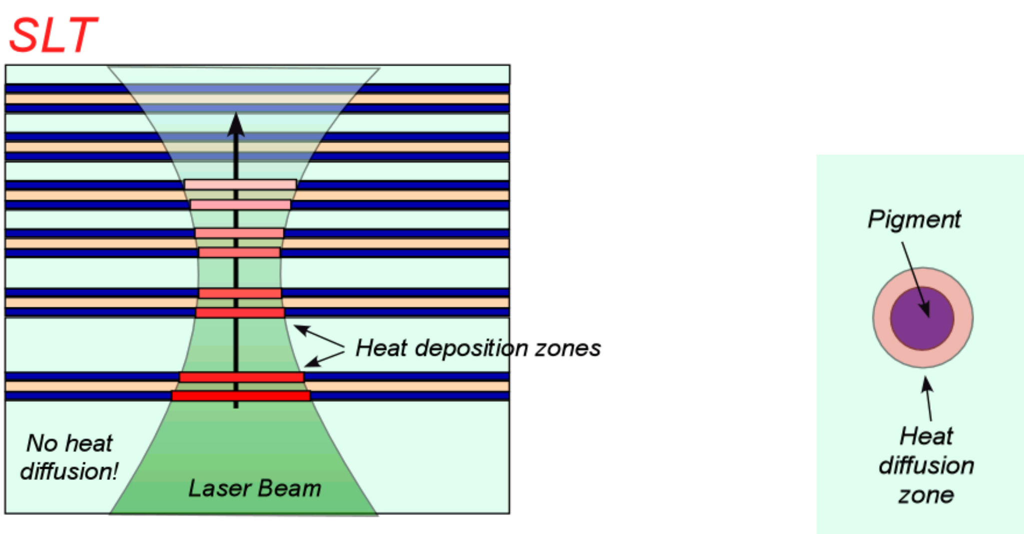

Figure 3: Predicted effect of SLT. The regions in bright red show the initial deposition of heat in the pigmented cell layers. Due to the short pulse duration, heat does not have time to diffuse outside the individual cells. The thermal effect is localized around the melanin granule (see insert).

In SOLX LT with the Alexandrite or Titanium Sapphire laser, the pulse duration is on the order of 8µs, which corresponds to a diffusion length of 2.6 µm. The estimated penetration depth in the TM at 780nm is 170µm. Heat will therefore be initially deposited over a larger volume of the TM than during ALT or SLT, since the penetration depth is approximately 4 times larger at 780nm than at 514 or 532 nm. During SOLX, heat will be less localized than during SLT. Heat may propagate to the trabecular beams and thermal shrinkage may be induced. But unlike in ALT, the shrinkage effect will be very localized (Figure 4).

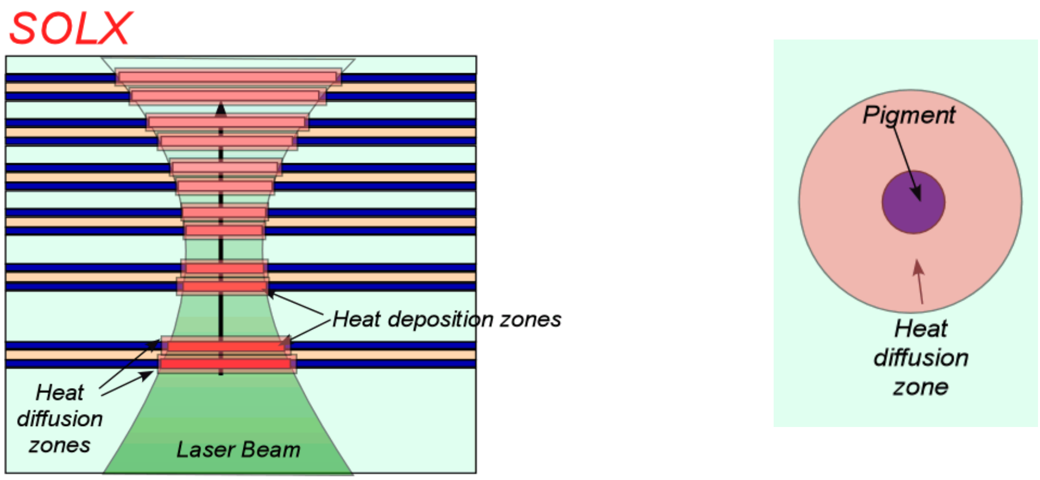

Figure 4: Predicted effect of SOLX LT. The regions in bright red show the initial deposition of heat in the pigmented cell layers. The initial heat deposition reaches deeper than during SLT or ALT. There will be more heat diffusion around the melanin granules than during SLT (see insert).

In summary, the preliminary qualitative thermal model indicates that the SOLX laser is expected to induce a significantly different thermal tissue effect than ALT or SLT. Because the SOLX laser uses infrared radiation, penetration in the TM will be deeper. On the other hand, because the pulse duration is longer than for the SLT laser, the effect will be less selective than during SLT, and may include a combination of both targeted cell death and localized tissue shrinkage or protein denaturation.