not model different tilt or rotation of the head around the visual axis between the input volumes. Such effects will introduce artificial motion that has to be modeled in order to register the input volumes. This additional motion is penalized by regularization. In a worst-case scenario, the penalty that is induced by these effects may prevent good registration. In practice, severe misalignment of the input volumes with respect to the pupil position and head rotation around the optical axis should therefore be avoided by consistent alignment by the operator when using the algorithm.

The presence of floaters or severe and changing vignetting also violates the assumption of the algorithm that an A-scan that was acquired at a given position in tissue has only image information that depends on the tissue. Depending on the amount of these effects in the data volumes, registration algorithm performance may be impaired. In addition, the current algorithm requires isotropically sampled raster scan input volumes. Extending the algorithm to non-isotropically sampled orthogonal raster scans or non-raster scan patterns would also be important for some future applications. Finally, the current method operates on OCT intensity data. It is possible to extend the method to also register and merge functional OCT imaging data, such as Doppler and polarization sensitive OCT.

It is also expected that the algorithm has limitations on the ability to correct motion artifacts depending on the overall signal to noise of the volume as well as the frequency and magnitude of motion artifacts. The data presented in this paper has relatively good input signal quality and moderate amounts of motion. Because evaluating algorithm performance requires acquiring and registering large numbers of data sets, the evaluation in this manuscript was limited to data from a single healthy subject, but with data acquired from multiple instruments and scan protocols. These examples are a proof of concept. Further investigations on the algorithm performance with low signal and high motion data sets from patients with retinal pathologies are necessary.

In conclusion, we believe that registration can play an important role in improving clinical OCT data quality and measurement reproducibility. These advances will be particularly important for the assessment of diseases such as glaucoma, age related macular degeneration and diabetic retinopathy, which require precise and reproducible measurement to track disease progression.

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