Supplementary:

Supplementary Table 1: Literature search-terms and -strategies

<table>
<thead>
<tr>
<th>Searchterms for OCT</th>
<th>Searchterms for automated analysis</th>
<th>Searchterms for AMD</th>
<th>Searchterms for retinal AMD biomarkers</th>
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<tr>
<td>OCT optical coherence</td>
<td><em>autom</em></td>
<td>age-related macular degeneration</td>
<td><em>drusen</em></td>
</tr>
<tr>
<td></td>
<td><em>compt</em></td>
<td>AMD</td>
<td><em>atroph</em></td>
</tr>
<tr>
<td></td>
<td><em>algorithm</em></td>
<td>ARM</td>
<td>GA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>epithel*</td>
</tr>
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<td></td>
<td></td>
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<td><em>pigment</em></td>
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<td>RPE</td>
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<td>lipofuscin</td>
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<table>
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<tr>
<th>Different possible search strategies</th>
<th>n</th>
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<td>#1 OCT (title) AND automated analysis (title)</td>
<td>470</td>
</tr>
<tr>
<td>#2 OCT (title or abstract) AND automated analysis (title or abstract)</td>
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</tr>
<tr>
<td>#3 OCT (title or abstract) AND automated analysis (title or abstract) AND AMD (title or abstract)</td>
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<td>#4 OCT (title or abstract) AND automated analysis (title or abstract) AND AMD-biomarkers (title or abstract)</td>
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The performed search was: #1 OR #3 OR #5 923

Literature search has been performed with the respective search terms (A) and the respective search formula (B). Indicated numbers are from the 31st of March 2016.
### Supplementary Table 2: Assessment of risk of bias

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<th>Reference</th>
<th>Patient selection</th>
<th>Index Test</th>
<th>Reference standard (1): every imaging beside OCT / expert’s diagnosis</th>
<th>Reference standard (2): manual OCT analysis</th>
<th>Flow and timing</th>
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<td>Drusen</td>
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<td>Sun et al. 2016</td>
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<td>Dolejší et al. 2010</td>
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<th>References</th>
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<td>Lee et al. 2012</td>
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</table>

References reporting accuracy for algorithms published elsewhere were also included and organized adjacent to the respected references. Not applicable items were left blank. Abbreviations: w/: with, pt: patients, GA: geographic atrophy, PED: pigment epithelial detachment, CAD: computer-aided-diagnosis.
### Supplementary Table 3. Generic image processing methods that are part of specific algorithms for AMD biomarker OCT analysis

<table>
<thead>
<tr>
<th>Name</th>
<th>Brief description</th>
<th>Detailed description</th>
<th>Algorithms for AMD biomarker analysis</th>
</tr>
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<tbody>
<tr>
<td>Active Contours</td>
<td>An initial contour is deformed, driven by external forces (attracting it to image features) and internal forces (encouraging plausible, e.g., smooth, contour shapes).</td>
<td>Kass et al. 1988⁸; Caselles et al. 1993⁹; Xu and Prince 1998¹⁰</td>
<td>Farsiu et al. 2008⁷; Jain et al. 2010⁹; Chen et al. 2013a¹³</td>
</tr>
<tr>
<td>Level Sets</td>
<td>Similar to active contours, but uses an implicit representation that enables topological changes, such as splits and mergers, or the representation of holes.</td>
<td>Sethian 1999¹⁰ and Gibou et al. 2003¹¹</td>
<td>Hu et al. 2013²⁷; Niu et al. 2016¹¹</td>
</tr>
<tr>
<td>Shortest Path Finding</td>
<td>A curve separating two retinal layers is found as a path between the left and right image boundaries that is both short and attracted to locations of strong image contrast.</td>
<td>Dijkstra 1959¹³</td>
<td>Chiu et al. 2012²⁵; Farsiu et al. 2014²⁶; Folgar et al. 2016²⁶</td>
</tr>
<tr>
<td>Graph cut (min-cut / max-flow)</td>
<td>Voxels are assigned to foreground or background so that a trade-off is achieved between local similarity to the respective region and a smooth overall segmentation. Technically, this is achieved by constructing a graph on the voxels and finding a minimum cut (max flow).</td>
<td>Boykov et al. 2001⁴⁹</td>
<td>Dolejší et al. 2010⁴²; Sun et al. 2016⁴⁹</td>
</tr>
<tr>
<td>Optimal Surface Detection</td>
<td>Simultaneously localizes multiple terrain-like surfaces in a volumetric image so that they are near an interface visible in the image, smooth, and separated by some minimum distance. Technically, this is similar to graph cuts, but the graph is constructed differently.</td>
<td>Li et al. 2006b⁶¹</td>
<td>Chen et al. 2012⁴⁸; Hu et al. 2013³⁷; Ding et al. 2013⁶¹</td>
</tr>
<tr>
<td>Multi-resolution Graph Search</td>
<td>An extension of optimal surface detection that first localizes surfaces at a coarser resolution, and uses their approximate location for fast detection at finer scales.</td>
<td>Lee 2009⁴⁷</td>
<td>Shi et al. 2014⁴⁰; Xu et al. 2015⁵⁴; Sun et al. 2016⁵⁹</td>
</tr>
<tr>
<td>Split Bregman Method</td>
<td>A fast optimization algorithm for a particular class of mathematical problems (“L1-regularized”). Among other things, it can be used to quickly segment an image into regions of similar intensity so that the boundary between regions is also short.</td>
<td>Goldstein and Osher 2009⁵³, Goldstein et al. 2010⁵²</td>
<td>Zheng et al. 2013⁴³; Ding et al. 2013⁶¹</td>
</tr>
<tr>
<td>Local Feature Based Classification</td>
<td>Feature vectors describing local texture, position, or shape are computed from the image, and local pathology is detected using supervised machine learning (such as Support Vector Machines, Random Forests, Bayesian or k Nearest Neighbors Classifiers).</td>
<td>Haralick and Shanmugam 1973⁵⁰</td>
<td>Liu et al. 2011b⁶⁹; Liu et al. 2011a⁶⁷; Chen et al. 2012⁴⁸; Serrano-Aguilar et al. 2012⁷⁰; Pilch et al. 2013⁵⁴; Albarrak et al. 2013²⁴; Zhang et al. 2014⁵⁵; Xu et al. 2015⁵⁶; Sun et al. 2016⁵⁹</td>
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<tr>
<td>Convolutional Neural Networks</td>
<td>Performs supervised classification without requiring pre-defined feature vectors; rather, features that facilitate detection are found automatically by the method itself.</td>
<td>LeCun et al. 1998⁵⁸</td>
<td>Schlegl et al. 2015⁵⁷</td>
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</table>