Improved visualisation of choroidal neovascularisation by scanning laser ophthalmoscope using image averaging

D U Bartsch, M H El-Bradey, A El-Musharaf, W R Freeman

Aims: To improve visualisation of angiographic features in patients with age related macular degeneration associated with choroidal neovascularisation (CNV) and related complications. To evaluate if image averaging can achieve this goal.

Methods: 27 eyes of 20 sequential patients with age related macular degeneration over a 3 month period were studied. Indocyanine green angiograms (ICGA), fluorescein angiograms (FA), and oral fluorescein angiograms were recorded with a confocal scanning laser ophthalmoscope. Software was used to average multiple images from a 10–20 image series (over 0.5–1.0 seconds). Image quality was assessed by two masked observers and graded on a scale of 0–3. A more quantifiable grading method was devised by adding a variable amount of Gaussian noise to the improved image until the original and image averaged image appeared equal.

Results: Masked review showed mild to strong improvement of visualisation of structures including borders of CNV. Improvement varied depending on the type and phase of the angiogram. Improvement was highest in late phase FA, mid and late phase ICGA, and all phases of oral FA.

Conclusion: Image averaging using software based algorithms improves the quality of angiographic images, particularly late ICGA images and oral FAs. This method may assist in the visualisation of choroidal neovascularisation in age related macular degeneration.

METHODS

Over a 3 month period, 27 eyes of 20 patients underwent angiography using intravenous (IV) FA, IV ICGA, or oral FA or a combination of several angiography methods. A total of 30 image sequences were recorded. Ten of these patients underwent IV ICGA, 10 underwent IV FA, and 10 oral FA. The cases were sequential cases and were not preselected. The patients were examined in the Jacobs Retina Center at the University of California San Diego (UCSD) Shiley Eye Center, Department of Ophthalmology. The Shiley Eye Center is a tertiary referral clinic for diseases of the retina. The human research protection program at UCSD has reviewed and approved this study.

We have used a confocal SLO (Heidelberg retina angiograph, HRA, Heidelberg Engineering Inc, Vista, CA, USA) to record FA or ICGA as well as infrared reflectance images. The instrument has been described previously and has four different laser wavelengths for illumination of the fundus (488 nm for FA excitation, 514 nm for red-free imaging, 795 nm for ICGA excitation, and 840 nm for infrared imaging). The HRA scans a laser point across the retina with the approximate size of 15 × 15 μm, the approximate lateral resolution of the eye. Since a one dimensional light detector is used, the inherent random noise is spread evenly.

Abbreviations: AMD, age related macular degeneration; CNV, choroidal neovascularisation; FA, fluorescein angiography; FOV, field of view; HRA, Heidelberg retina angiograph; ICGA, indocyanine green angiography; IV, intravenous; RPE, retinal pigment epithelium; SLO, scanning laser ophthalmoscope; SNR, signal to noise ratio
Improved visualisation using image averaging

Table 1  Study population

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of eyes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active choroidal neovascularisation</td>
<td>14</td>
</tr>
<tr>
<td>associated with AMD</td>
<td></td>
</tr>
<tr>
<td>Disciform scar or old inactive CNV</td>
<td>3</td>
</tr>
<tr>
<td>Dry AMD with drusen</td>
<td>8</td>
</tr>
<tr>
<td>Macular pathology</td>
<td>2</td>
</tr>
<tr>
<td>AMD, age related macular degeneration; CNV, choroidal neovascularisation.</td>
<td></td>
</tr>
</tbody>
</table>

after unmasking if the image averaged image was judged to be of higher quality than the non-averaged image, otherwise a negative score was recorded. The mean improvement of each image pair we determined if one image was mildly (grade 1), moderately (grade 2), or highly superior (grade 3) after unmasking if the image averaged image was judged to be of higher quality than the non-averaged image, otherwise a negative score was recorded. The mean improvement of each phase and type of angiogram and statistical significance by one sample t test was determined.

RESULTS

Thirty image sequences were recorded in 27 eyes of 20 sequential patients with age related macular degeneration over a 3 month period (table 1). Of these 27 eyes, 14 had active CNV associated with AMD. Three eyes had disciform scars or old inactive choroidal neovascularisation. Eight eyes had dry AMD with drusen and were examined by angiography to rule out CNV. An additional two eyes had macular pathology associated with AMD.

The results of the subjective grading by two ophthalmologists are shown in table 2. There was significant improvement in all groups and all phases. In the early phase (fig 1) of the IVFA five out of 10 subjects showed significant improvement (p<0.05) while seven out 10 subjects showed significant improvement in the IVFA mid-phase (p<0.01). In the early phase of the ICGA (fig 2) eight out of 10 subjects showed significant improvement (p<0.01) while nine out 10 subjects showed significant improvement in the ICGA mid-phase (p<0.001). The improvement was also highly significant (p<0.001) in the late phase of FA (fig 3), the mid and late phase of ICGA, and all phases of the oral FA (mid-phase: fig 4, late phase: figs 5–7). It has to be noted that the appearance of the choroidal circulation was particularly improved (figs 2–7). The speckle-like noise that is present in the original images was largely absent in the averaged images.

The accuracy of the motion correcting image alignment process can easily be evaluated by the appearance of the major blood vessels in the aligned image. If the alignment was successful, no double blood vessels appeared around the optic nerve head. Unsuccessful correction of lateral or rotational motion was characterised by the double
appearance of one or more blood vessels. We did not observe any unsuccessfully aligned image series in this study.

The results of our more quantifiable image evaluation technique are shown in table 3. The numbers indicate the amount of noise that was added to the image averaged image to make it appear equal to the raw noisy image. Thus, a higher number indicates that the image averaged image had less noise and was thus of higher quality. The results show that the more quantifiable image evaluation and comparison method follows the trend of the subjective grading results shown in table 2. The images with the highest improvement were recorded in the late phase of the FA, late phase of the ICGA, and all phases of oral FA.

DISCUSSION
CNV associated with AMD is treatable but often with poor results. Feeder vessel treatment has been evaluated; however, such vessels often are difficult to discern. Improved visualisation of CNV might be of benefit in allowing improved classification of the disease, and earlier or better treatment. For this reason we wanted to determine whether image averaging would improve visualisation of CNV in patients with AMD. In addition, oral FA has recently been shown to provide clinically useful images in many eyes and we wished to determine if image quality could be improved. Even in eyes without CNV but with pre-neovascular lesions it can be very important to rule out CNV and poor image quality can make this difficult.

In our study we found that image averaging significantly improves image quality in a subjective, four level grading examination and a more quantifiable, Gaussian noise additive grading examination. The improvement is real, albeit modest in the early and mid-phase of the angiograms. The improvement may be clinically useful.

Image averaging reduces noise, but loses some temporal information. Rapid changes occur only during the arterial inflow phase and we did not attempt image averaging in this phase. Furthermore, as every ophthalmologist is aware, the image quality in the inflow phase is usually sufficient and would not benefit from image quality improvement.

Image averaging is a standard technique used in all areas of medical imaging for improving images. A theoretical analysis shows that the improvement of the SNR in the averaged image increases with the square root of the number of images. This was confirmed in a three dimensional reconstruction of an electron microscopy tomography study.
Improved visualisation using image averaging

and in magnetic resonance imaging studies. Some authors have reported problems with the technique in the presence of motion artefacts. The main problem is that uncompensated motion artefacts degrade the image rather than allow image improvement. Our experience was similar with non-aligned or poorly aligned image series. However, the presence of the automated cross correlation image alignment enables us to align movement. The inability of the software to align some images can easily be spotted by the appearance of double images in the blood vessel structure.

The main problem in the acquisition of angiographic images is the low fluorescence in the late phase of both FA and ICGA. Other problems are the poor resolution caused by the aberrations in the eye and the light safety limits. Thus, improved optics, or improved detectors, or improved dyes can improve visibility. Adaptive optics has not only the potential to improve resolution, but should also improve the SNR as more light from the retina is collected at the light detector. Since light levels in adaptive optical imaging are limited by the same rules as in our present study, image averaging is a useful and helpful method that should be employed as a routine imaging method in digital retinal imaging. Future improvements to the image averaging technique include improved automated cross correlation with detection and automatic rejection of unaligned images and inclusion of eye trackers.

Image averaging improved image quality for all phases of oral and intravenous fluorescein angiography and intravenous ICG angiography. Improvement in image quality is most pronounced in the late phase of the angiograms. The improvement also depends on the type of angiography that was studied. The improvement was least in intravenous FA and best in oral FA. For ICG angiography there was also striking improvement in late phase image quality.

We believe that the degree of improvement depends on the initial quality of the acquired image. IV FA has an inherent high quality in the early phase. In this case image averaging can only produce a marginal improvement. Oral FA and ICGA are subject to more noise influence that can be ameliorated with noise reducing techniques such as image averaging. Our group and others have recently used oral FA for imaging patients with AMD and diabetic retinopathy. Newsom and associates have used "local contrast enhancement" to improve image quality in oral FA. Thus, new types of imaging methods in ophthalmology require new image processing tools. In theory, the use of image averaging is only limited by image registration problems and the increase in dynamic range as a result of the additive nature of the averaging process.

In conclusion, image averaging offers a simple yet effective method to significantly improve image quality for clinical diagnosis in angiography. This technique merits further investigation.

| Table 2 Magnitude of improvement in subjective image quality assessment (SD) |
|-----------------|-----------------|-----------------|-----------------|
| Angiogram type  | Number of images| Early phase     | Mid-phase       | Late phase      |
| IV FA           | 10              | 0.80 (0.92)**   | 1.00 (0.82)**   | 2.10 (0.99)**   |
| ICGA            | 10              | 1.20 (0.79)**   | 1.80 (0.92)**   | 2.30 (0.48)**   |
| Oral FA         | 10              | 1.56 (0.68)**   | 2.22 (0.83)**   | 2.44 (0.53)**   |

Scale: Grade 0 means that both images were of equal quality. For each image pair we determined if one image was mildly (grade 1), moderately (grade 2), or highly superior (grade 3) *p<0.05 in one paired Student t test comparing to null hypothesis. **p<0.01 in one paired Student t test comparing to null hypothesis. ***p<0.001 in one paired Student t test comparing to null hypothesis.

| Table 3 Magnitude of improvement in quantitative image quality assessment (SD) |
|-----------------|-----------------|-----------------|-----------------|
| Angiogram type  | Early phase     | Mid-phase       | Late phase      |
| IV FA           | 15 (8.9)        | 17.5 (13.4)     | 21.5 (13.4)     |
| ICGA            | 15.3 (6.5)      | 15.3 (6.4)      | 18.8 (10.3)     |
| Oral FA         | 19.8 (9)        | 16.1 (7.8)      | 22.7 (6)        |

Scale: The improvement is given in arbitrary units. Adobe Photoshop version 5.5 (Macintosh) was used to add Gaussian noise. The variable amount of noise that can be added ranges from 0 to 999 units.

REFERENCES

Authors' affiliations
D U Bartsch, W R Freeman, Jacobs Retina Center, Department of Ophthalmology, University of California San Diego, CA, USA
M H El-Bradey, Faculty of Medicine, Tanta University, Egypt
A El-Musharaf, Toronto, Canada

Sponsor details/grant support: This study was sponsored in part by a grant from the National Eye Institute NIH-NER grant #EY13304 (DUB) and NIH grant #EY07366 (WRF) and Research to Prevent Blindness (UCSD).

Competing interests: The UCSD Shiley Eye Center has received unrestricted research support from Heidelberg Engineering, a company that makes the confocal scanning laser ophthalmoscope used in this study.

Ethics approval: The Human Research Protection Program at UCSD has reviewed and approved this study.

www.bjophthalmol.com


Improved visualisation of choroidal neovascularisation by scanning laser ophthalmoscope using image averaging
D U Bartsch, M H El-Bradey, A El-Musharaf and W R Freeman

Br J Ophthalmol 2005 89: 1026-1030
doi: 10.1136/bjo.2004.057364

Updated information and services can be found at:
http://bjo.bmj.com/content/89/8/1026

These include:
References
This article cites 30 articles, 2 of which you can access for free at:
http://bjo.bmj.com/content/89/8/1026#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections
Choroid (565)
Retina (1608)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/