



# Digital FA & ICG Overlay Using Green Pre-treatment Retinal Images Enhances Treatment Accuracy of CNVM's



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## Introduction

Digital overlay technology can be used to correlate suspected CNVM lesions in alternate angiographic representations (FA to ICG or reversed) or to locate the angiographically suspected lesion on a PRE-TREATMENT GREENFILTERRETINALPHOTOGRAPH (FA or ICG to green photograph).

We overlaid FA and ICG angiograms onto PRE-TREATMENTGREENDIGITAL PHOTOGRAPHS to improve therapeutic accuracy.

We then examined the overlay confidence level between angiographic frame pairs and angiographic/GREENFILTERIMAGE pairs.

## Methods

- 314 eyes with suspected CNVM's underwent GREENDIGITALPHOTOGRAPHY, FA &/or ICG.
- Hyperfluorescent angiography lesions were traced (CASE 1) and overlaid on a PRE-TREATMENT GREENIMAGE. Patients were randomized to therapy with and without overlay.
- The confidence level of the overlay between the ICG and the PRE-TREATMENTGREEN PHOTOGRAPHY was then compared to the confidence level of the overlay between the ICG & FA images.

The 'overlay' function of the commercially available OIS Digital Angiography System [software version 2.4\* (\*Version 4.0 has recently become available)] was used to compare images. The overlay process is performed in the '4-up' mode using 1024x1024 pixel images which have been scaled to 512x512. In this semi-automatic system, the user defines a 'starting point' within the inner 2/3 of the image, then the computer performs a first order warp (image pair matched for rotation and translation using 3 points) on the surrounding 128x128 pixel square within a vessel enhanced version of both images. After this initial alignment, a second order warp (image pair matched for rotation, translation, and curvature) is attempted, and 36 regularly spaced computer selected areas (128x128 pixel square) are compared.

Confidence is rated at LOW when only the single selected point matches; MEDIUM when only the first order warp is successful; HIGH when the second order warp is successful but there is a low correlation between the image pairs; or VERY HIGH when the second order warp is successful and there is significant correlation between the computer selected image pairs.

- 2 masked observers independently performed multiple overlays on 32 angiograms from 16 patients who had FA and ICG angiography on the same day.

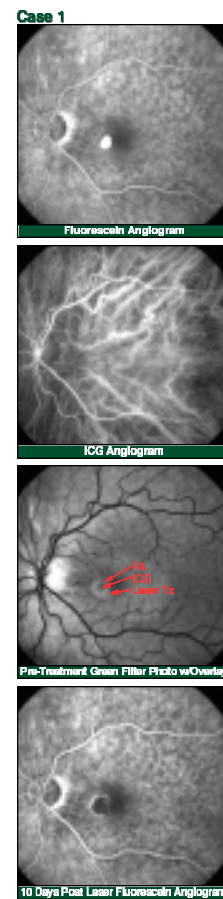
- Angiographic frames selected for overlay paired as follows:
  - a GREENPRE-TREATMENTPHOTOGRAPH and the earliest frame from ICG angiography on which pathology could be identified (range 1:31 - 11:38 minutes, median 2:54 minutes)
  - the same ICG frame and an early transit phase FA frame (range 0:25 - 1:42 minutes, median 0:32 minutes)

- 9 different 'starting points' in each image pair were selected to start the overlay

- 3 'starting points' in each pair of overlays were chosen at:
  - obvious vessel bends
  - vessel crossings
  - vessel bifurcations

- Overlay accuracy ratings were recorded

- Numerical equivalents were assigned to the verbal ratings:
  - Very high = 4
  - High = 3
  - Medium = 2
  - Low = 1



## Results

- We observed the full range of confidence levels from low to very high. The mean confidence level for ICG/GREEN overlays was 2.68. The mean confidence level for ICG/FA overlays was 2.17.

- The confidence level for the ICG/GREEN overlays was higher when compared to the confidence level of ICG-FA overlays (p=0.0001).

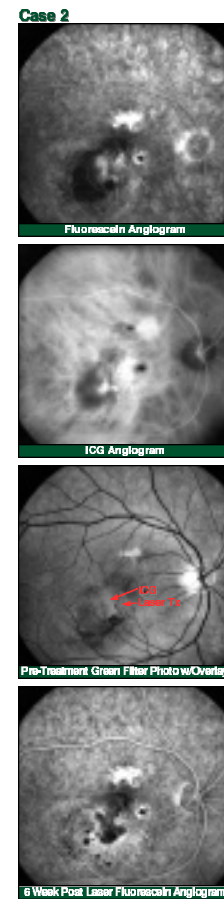
- While not statistically significant, there was a trend toward higher confidence level when vessel crossings were used as the starting point.
  - vessel crossings (mean = 2.46, median = 2.33)
  - obvious vessel bends (mean = 2.40, median = 2.17)
  - vessel bifurcations (mean = 2.40, median = 2.17)

- There was no statistically significant difference in confidence level by observer.

- We observed that selected eyes with ill-defined lesions on fluorescein angiography (CASE 2) became more frequently treatable using GREENPRE-TREATMENT overlays from ICG angiography, depending upon tie-point reliability.

CONFIDENCE LEVEL					
BY MATCHING LOCATION, OBSERVER AND MATCHING IMAGE					
Variable	Mean	Median	S.D.	95% Conf. Interval	p-value*
Matching location					
obvious vessel bends	2.40	2.17	0.911	2.18-2.63	0.710†
vessel bifurcations	2.40	2.17	0.914	2.17-2.62	0.674
vessel crossings	2.46	2.33	0.904	2.23-2.69	
Observer					
# 1	2.43	2.33	0.897	2.25-2.61	0.884
# 2	2.41	2.33	0.919	2.23-2.60	
Matching image					
ICG/green	2.68	3.00	0.960	2.50-2.85	0.0001
ICG/FA	2.17	2.00	0.881	1.99-2.34	

\* By paired t-test  
† Comparison between obvious vessel bends and vessel crossings  
Comparison between vessel bifurcations and vessel crossings



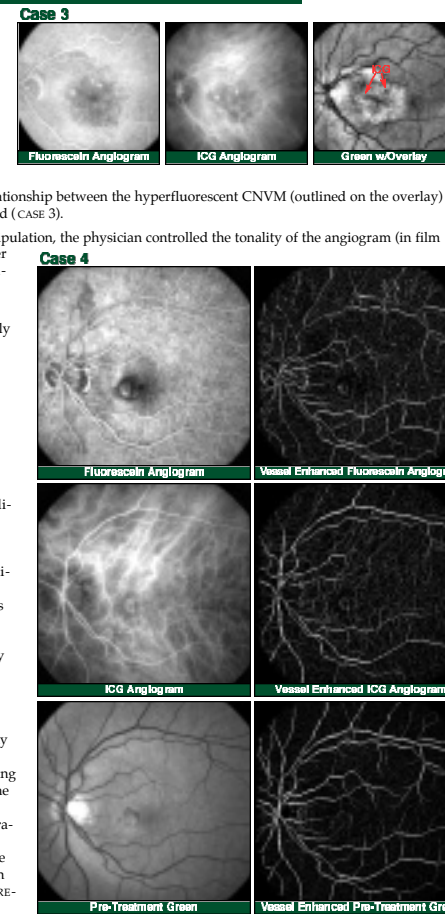
## Discussion

Using the digital overlay technology, physician treatment decisions were more rapid, predictable, and accurate:

- Treating from the GREEN IMAGE with overlay information (as opposed to the FA images) enabled the physician to better visualize the relationship between the hyperfluorescent CNVM (outlined on the overlay) and retinal fluid, blood, or lipid (CASE 3).
- By using digital image manipulation, the physician controlled the tonality of the angiogram (in film angiography, the photographer determines the tonality by controlling the photographic process).
- The GREENIMAGE was visually closer to the retinal image viewed during treatment, streamlining treatment decisions.
- The larger size of the on-screen digital proof sheets improved the ability of the physician to interpret the angiogram relative to smaller film images which require additional magnification.

While two angiographic images may seem visually similar (CASE 4), it is in fact a set of enhanced high contrast images which the computer actually compares.

We postulate that the overlay confidence level was higher in the ICG/GREENPRE-TREATMENT images because they exhibit a similar level of retinal vessel detail. Fluorescein angiography increases the apparent level of retinal vascular detail, increasing the background detail when the major retinal vessels are enhanced. Fluorescein angiography's prominent background details match less well with the subdued background details in ICG angiography and GREENPRE-TREATMENT photography.



## Clinical Suggestions:

- VESSEL CONFIGURATION CHECK (VCC)**  
Judge the visual accuracy of the overlay by performing a Vessel Configuration Check (VCC). Use the 'Trace' function to outline a nearby vessel pattern to confirm overlay accuracy.
- IMAGE QUALITY**  
Full tonal range images with moderate to high contrast increased confidence levels. Balance the exposure, camera sensitivity, and the digital system contrast for a broad tonal range. Consider enhancing low contrast images to increase confidence levels.
- SIMILARITY**  
Like 'field definition', magnification, and level of focus increased confidence levels. Use photographic techniques which enhance consistent fixation.
- PROXIMITY**  
VCC's were more consistent when 'starting points' and overlays were chosen near the area of concern (CASE 5).
- MANIPULATION**  
Different clinicians may prefer different image enhancement procedures. Ophthalmologists using digital angiography systems should be aware of the type, degree, and effect of digital manipulations available and their influence on the validity of the angiographic information.
- ACCURACY**  
Current digital overlay technology is better than previous film based 'stare and compare' technology. However, regardless of the specific confidence level the digital angiography unit suggests, ophthalmologists should continue to use their clinical judgment and experience to guide laser treatment.

## Conclusions

- The confidence level of the digital angiography overlay was higher when ICG and GREENPRE-TREATMENTANGIOGRAMS were overlaid, as opposed to ICG and FA angiography pairings.
- Marginally higher confidence overlays are obtained when the 'starting point' chosen is on a vessel intersection, as opposed to a vessel bifurcation or an obvious vessel bend.
- Overlay tracing of both FA and ICG choroidal hyperfluorescent lesions onto the pre-treatment green digital image maximized visualization of retinal vascular detail, enhancing accuracy of laser treatment margins.