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Enhancement of Retinal Images: Pros and Problems

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PELI, E. *Enhancement of retinal images: Pros and problems.* NEUROSCI BIOBEHAV REV 17(4) 477–482, 1993.— Evaluation of retinal images is essential to modern ophthalmic care. With the advent of image processing equipment, digital recording and processing of retinal images is starting to replace the standard film based fundus photography. The ability to enhance images is cited as one of the major benefits of this expensive technology. This paper critically reviews the practices employed in the image enhancement literature. It is argued that the papers published to date have not presented convincing evidence regarding the diagnostic value of retinal image enhancement. The more elaborate studies in radiology suggest, at best, modest diagnostic improvement with enhancement. The special difficulties associated with the demonstration of an improved diagnosis in ophthalmic imaging are discussed in terms of the diagnostic task and the selection of study populations.

Image enhancement Fundus Retina Digital processing Diagnosis Technology Ophthalmic

RETINAL images are routinely used in ophthalmic practice for diagnosis and follow-up of eye diseases. Retinal photographs are of great value to ophthalmic practitioners for detecting subtle fundus changes that may occur over time. The quality of the retinal image is frequently reduced by the specular reflections from the cornea and lens and light scatter from cataracts or other ocular media turbidity. This degradation of image quality may greatly impede visual inspection and automated image processing of the photographs.

Various techniques to improve fundus visibility in the presence of media turbidity have been investigated. Commonly, the optical system was designed to separate the illumination and imaging pathways at the patient's pupil (the Gullstrand principle) to reduce specular reflections and backscatter from the cataract (16). Modification of the photographic technique and the use of various filters may be helpful (9). However, even with the best imaging techniques, cataracts may degrade the image significantly. In the presence of moderate turbidity, the general appearance of the retina is clear, but very fine details, such as the retinal nerve fiber layer or small arteries in fluorescein angiography, are difficult to evaluate. In recent years digital image-enhancement techniques have been used in an effort to improve the visibility of fundus details from photographs taken through relatively clear media (11,27,37, 44) and through cataracts (30,31).

Image enhancement algorithms are usually classified as noise removal/restoration methods or as contrast enhancement techniques, including both spatial filtering and gray level modification methods (17,32). In some cases, a combination of both types of enhancement are applied. Image enhancement may be used as a preprocessing stage for automated computerized image analysis such as the automated detection of lesions in images (15). For the purpose of this paper, however, enhancement is defined more narrowly as the processing of images designed to improve human observers' performance in evaluating those images.

In this paper the value of image enhancement is examined critically. A number of practices used by many in the field, including the author, are questioned, and attempts are made to establish a more stringent requirement for the presentation of image enhancement techniques. Specifically, I argue that the results of new enhancement algorithms should be presented in a way that clearly demonstrate the value-added benefit of the new algorithm over commonly available simple and fast enhancement methods; the use of enhancement and restoration algorithms should be demonstrated with real degraded images rather than with simulated images; the value or contribution of the enhancement to increased diagnostic power should be demonstrated by measurement rather than inferred from "before and after" presentation. It appears that little evidence of such improvement is available in the radiology field, where such techniques have been used extensively, and I know of no such investigation applied to fundus images.

BEFORE AND AFTER PRESENTATION OF THE RESULTS OF ENHANCEMENT

Presentation of image enhancement results in medical as well as all other fields is frequently limited to the side-by-side comparison of the original unprocessed image with the enhanced image (17,27,34,42). The presented images are presumed to speak for themselves so that the reader may appreciate the improvement. Medical images of all kinds, fundus images included, may vary considerably in their gray level histogram due to exposure differences and other factors and, thus, may be difficult to compare side-by-side. One way to reduce this difficulty is to normalize all images to be compared to the full gray level range of the display before enhancement or other processing is applied (15). However, this operation tends to reduce the apparent added benefit of the enhancement achieved with spatial filtering and other methods, and, therefore, has traditionally been avoided (30).

We have used side-by-side presentation in our studies of the enhancement of the retinal nerve fiber layer (RNFL) (22,27). The fine striations of the normal RNFL are difficult to observe in fundus photographs, especially when the patient's fundus pigmentation is light or when the ocular media is not clear (29). It is, therefore, difficult to detect the subtle loss of striated patterns that occur in many diseases of the optic nerve. We reported that histogram modification techniques appear to improve the visibility of wedge defects, while spatial filtering methods increase the visibility of fine slit defects as well as the visibility of the normal RNFL striations (27). We noted that we were able to detect in the processed images lesions as well as normal striations that were not detected in the original. These results were interpreted to suggest that enhancement can be a useful diagnostic tool. However, we have also realized that once these findings were noted in the enhanced image they were easy to observe in the original image as well. This last observation puts into question the diagnostic value. In addition, it compromises the reader's judgment as (s)he sees both images at the same time. What is lacking in this commonly used mode of presentation is a formal measurement of the difference in detection performance using the two images.

Such casual presentation of results is generally unacceptable in other types of scientific investigation. It has probably been permitted to persist in the area of image enhancement because of our common belief that "a picture is worth a thousand words," and our reliance on believing what we are seeing. Unfortunately, often what is printed in a scientific journal is quite different from the image presented on a video screen. Typically, the low dynamic range of the printed picture tends to artificially increase the effect of the demonstrated enhancement by failing to reproduce in the printed image details that are visible on the displayed image.

Comparison with Results of Simple Enhancement

The enhancement of images taken through cataracts falls into the category of image restoration. If done effectively, it may be very useful, because most serious eye diseases are associated with old age and, therefore, are frequently accompanied by incipient or mature cataracts. Peli and Schwartz (31) used side-by-side presentation in a study of the enhancement of retinal images taken through cataracts. In this case we were able to point to the ability to detect a change in small vessels. These changed vessels were essentially unnoticeable in the original, unenhanced image. Such shifts in the path of the circumlinear vessels are an indicator of increased cupping and, therefore, are important in the diagnosis and followup of glaucoma. Formal comparison of diagnostic task performance would probably demonstrate improvement with the enhanced images as compared with the unprocessed original images in this case. However, it is not clear whether this is the proper comparison to make. I would like to claim that the vascular patterns and, therefore, the clinically relevant changes, would also be visible with a simple histogram modification such as histogram equalization, or even with a look-up table modification such as windowing. Thus, even when the value of image enhancement can be demonstrated, the value of new algorithms should be compared with the performance obtained with well-known, widely available, and computationally inexpensive procedures, rather than comparing them with the raw image.

More complicated processing, such as the Wiener filtering proposed by Peli and Peli (30) may be intellectually challenging. The model developed in the process may serve a useful purpose in improving our understanding of the imaging, and image degradation processes in the eye, and, in this specific case, the enhancement may actually aid diagnosis. However, the value added by the new method should be evaluated by testing it against some other enhancement rather than against the original image, and in a more definitive way than with the side-by-side display or printing of images. Hunt (13) claimed, based on his many years of experience, that if image restoration problems can be solved at all, then in about 75% of the cases the images can be treated with some of the simplest techniques. Only about half of the remaining 25% may be solvable. He suggested that an important area of research will be to identify the types of images that cannot be successfully restored with current techniques.

Image Comparisons on Nonlinear Displays

The luminance emitted from a cathode ray tube (CRT) display is a nonlinear function (the gamma function) of the input video signal voltage. The nonlinearity usually is approximated by a power law, $L = v^{\gamma}$. The value of the exponent γ, for most displays, ranges from 2.2 to 2.5. (A gamma value of 2.2 was assumed as a standard for the NTSC system.) This nonlinear transformation results in compression of the dark luminance levels and expansion of the bright luminance levels. In a recent paper, the consequences of displaying the result of image enhancements on a nonlinear screen were described (23). For example, in homomorphic filtering (21) the image is compressed by a logarithmic transformation, high-pass filtered, and then antilogged before presentation. Schreiber (36) argued against the explanation of the effect of the homomorphic filter advanced by the developers of the algorithm and suggested that a significant enhancement effect will occur only with unusual images such as the boiler room image used by Oppenheim et al. (21) and others. I argued that even for these extreme cases some of the dramatic effects of image improvement obtained with homomorphic filtering are not necessarily a result of the proposed processing. Instead, much of the effect can be achieved simply by shifting the working point up on the nonlinear gamma curve (23). To illustrate this point I processed the boiler room image by simply increasing the luminance at the dark end and keeping the bright end fixed. This look-up table transformation reduces the contrast at every level of the stored image, but more significantly at the low luminance levels. Yet, as can be seen in the image displayed on the nonlinear screen, the details in the low luminance areas are highly enhanced [Fig. 7 in (23)]. Similar transformations of the low luminance mean were included explicitly in the adaptive enhancement of this image (32) and in the original processing by homomorphic filtering (21).

When evaluating the effect of enhancement using either side-by-side presentation or more formal testing, a linear display should be used. Using a linearized screen permits image processing and enhancement to be achieved without concern for the specific display to be used (33). It is now frequently used in radiology and should be adapted for ophthalmic images. The use of a linearized display is not without problems, however. Frequently the 8 bit luminance value will not be sufficient for proper representation of the linearized display (23,43) especially at the low end of luminance values.

SIMULATED DEGRADATION

The effects of image enhancement and restoration techniques are frequently demonstrated using simulated image degradation (17,41). The general approach in such cases is to take an image and apply to it the type of degradation, which is assumed to take place in the actual imaging situation. This can be done by adding or multiplying noise (Gaussian or otherwise) (17), by gray scale manipulation (41), or by other transformation (i.e., simulating motion or blur) (12). The degraded image than undergoes enhancement or restoration and the results are either displayed side-by-side or, in many cases, presented as the calculated mean square error (or the mean absolute error) between the restored and the original image (4).

The use of simulations of image degradation in textbook demonstrations and teaching is appropriate. Such simulations may also be useful in debugging and testing the software. However, their value in demonstrating the effectiveness of the enhancement for any practical purpose is questionable. It stands to reason that an algorithm that was designed to remove Gaussian white noise will perform well when operating on a simulated image where Gaussian white noise has been added. However, the assumption that images are degraded by white Gaussian noise in the imaging systems is frequently based only on our ability to analytically address such noise, rather than on any measurements or indications.

The use of simulated degradation in image restoration techniques enables the investigator to evaluate the restoration process using direct measures such as the mean square error. When actual degraded images are used, such an evaluation is usually impossible, even if a clear, undegraded image of the same scene is available. The two images to be compared with such a measure have to be perfectly aligned, and such alignment is rarely possible. The images may be realigned using one of many image registration methods (6,24); however, the accuracy of the registration is limited by the quality of the restoration, among other factors.

The evaluation of the effectiveness of enhancement for the purpose of restoring degraded images requires access to undegraded images. Such images are not always available. When enhancement of earth images taken through cloud cover are evaluated, images taken on a clear day can be used for comparison. In the case of fundus imaging through cataracts or other media opacities, a clear image may be available. Such images may be on file (taken before cataract development), or may be obtained following cataract surgery. Image pairs of this sort may be used to evaluate the effectiveness of the restoration process. Peli and Peli (30) have used the precataractous image as part of the estimation process used in the design of the Wiener filter applied. We demonstrated improvement with a side-by-side comparison and have found that the filtering process utilizing the clear precataractous images was better than the results obtained without them. However, we have not tested the effect of replacing the patients' precataract image with a clear image of any other eye.

DOES ENHANCEMENT IMPROVE PERFORMANCE?

Lessons from Radiology

Image enhancement would be considered a valuable asset if it could improve performance. Such improvement would be demonstrated if a trained observer could perform a diagnostic or patient management task more effectively using the enhanced images. The ability of observers to perform with the aid of an imaging method depends on the quality of the information available to the observer. The receiver operating curve (ROC) analysis (40) is considered the best method for representing the potential discrimination performance of an imaging modality without the problems of observer bias. In radiology, where digital images and, therefore, image enhancement have been used for many years, the success of image enhancement found in such investigations was modest at best.

Using simulated radiological images with simulated lesions in one of 18 possible locations, Ishida et al. (14) found statistically significant improvement in detection when using overall contrast enhancement. In this experiment, a square target of uniform intensity was added to a uniform but noisy digitized background. The contrast of the image was increased by rescaling, and new films were produced to be presented to observers. Although the results indicate improvement in detection, the relation between this effect and improvement in a clinical setting is not clear. One important factor that was missed in this paradigm is the masking effects of the structured radiological image and the uncertainty in target position over the whole image.

Zimmerman et al. (46) compared detection of artificial lesions introduced digitally into clinical CT images of the chest. They compared observers' performance using the automated adaptive histogram equalization (AHE) vs. a simple, manually driven intensity windowing technique. They found little difference in performance between the two imaging modes. Thus, the complicated AHE, which takes 2 h on VAX 11/780, or the approximated AHE, which takes about a minute on a micro computer for a 512 × 512 image, is not better than the simple real-time look-up table manipulation of intensity windowing. Note that in this carefully designed study the performance with the AHE was not compared with the unprocessed image. Rather, an available, computationally efficient alternative was tested. The use of simulated lesions allows parametric evaluation of performance with different levels of lesion visibility, and the convenience of a clearly known lesion in a known position. However, the authors noted that the type of lesion used was so difficult to detect even in the enhanced images that most such lesions would go undetected in a typical clinical situation. Thus, even the results of this apparently clinically relevant study are not easily translated to practical decisions regarding the potential value of image enhancement in practice.

A different type of simulated lesion using tissue equivalent paraffin nodules placed over the chest of normal patients yielded similar results (20). In that study the effects of five different enhancement methods, including edge enhancement and contrast reversal, on detection were evaluated with five trained readers. The images in that study were directly acquired digital radiographs, rather than the digitized films used in most previous studies. As in most other studies, no significant difference was found in detection performance [area under the receiver operating curve, ROC (18)] compared with detection from the unprocessed image.

Because such studies of observers' performance with various imaging modalities are so complicated, Barrett (3) and his co-workers have advanced a linear discriminant model for computation of observers' performance on various tasks using various images. Their model predicts no effect of histogram manipulation of any sort on the detectability of lesions. In a study to test their model (45), they found that the psychophysical results are the same for human observers. It should be noted that this model is relevant only for binary detection and discrimination tasks.

The results with actual radiologic images of clinical cases are quite varied, but are generally discouraging. Oestmann et al. (19) showed, with images of subtle lung cancers compared with normal chest films, that edge enhancement impaired diagnostic accuracy even with high resolution display. Similar results were reported by others [reviewed by Rosenthal et al. (35)]. Only one study I am aware of reported detection improvement with contrast modification using scale reversal as the method (38). Scale reversed CT images were also found to have the most natural anatomic appearance (7). Rosenthal et al. (35) have compared experienced radiologists' diagnostic performance using digitized chest radiographs with their performance using various contrast enhancement and edge enhancement methods. They found no significant difference in diagnostic performance with or without enhancement for any of the three abnormalities included.

The Ophthalmic Case

I am not aware of any studies directly evaluating the diagnostic value of enhancement of fundus images or any other ophthalmic images. In fact, no such studies have been performed to evaluate the diagnostic value of various ophthalmic imaging methods such as fluorescein angiography, indocynine green angiography, or scanning laser ophthalmoscopy. A few comparative studies of various parameters of fundus photography (e.g., films, processing, cameras, and filters) were generally limited to side-by-side presentation of the results (1, 8,37). Evaluation of various photographic parameters were also limited to evaluating observers' subjective preference for the different modes of presentation (29) rather than demonstrating improved diagnostic value directly. Most studies of image processing applications to ophthalmic images have typically been limited to an evaluation of the reproducibility of the processing method (2,5,28). Other studies were limited to an evaluation of the ability of the measured parameters to classify patients who could be classified clinically.

ENHANCEMENT AS A CUEING AID

Image enhancement per se may prove of limited value in improving observers' ability to detect or discriminate clinically relevant details in fundus images. This appears to be the result of the superior ability of trained observers, given sufficient time, to detect lesions from the original image as well as from any enhanced images. In a clinical setting, however, the observers' time is not unlimited. Thus, a method that can decrease the time needed for the same level of performance is also of great value. Unfortunately, like many others before them, Rosenthal et al. (35) also reported that the time required by the radiologist to read processed images increased significantly (by as much as 50%). However, manually controlled windowing, now frequently used, also takes time from the radiologists. Therefore, the search for a better method continues.

Computerized image processing may be useful as a visual aid to diagnosis if used differently. The processing of digital images to detect or discriminate lesions may be used as a cueing aid for the trained observer. By directing the observer's attention to suspicious areas in the image, search time may be reduced and the yield increased. As the consequences associated with misses in medical diagnosis are frequently more severe than the consequences of false alarms, such cueing methods should usually be designed to provide 100% detection. Such a high rate of hits comes at a cost of increased false alarms, which may then be rejected by the human observer (15).

What to Cue for in Fundus Images

Little is known about the effects of the cueing approach in radiology or other medical images. However, the discussion of such possible approaches calls attention to a distinct difference between the typical analysis of radiological images and the evaluation of fundus images. While in radiology the detection of a lesion is most commonly the task, in fundus images there is no such clear task. Of course, lesions need to be detected and differentiated, but in most cases the ophthalmologist's task is less clearly defined. In many cases, multiple lesions may be present, such as drusen and pigmentary changes in age-related maculopathy, or aneurysms, hemorrhages, and exudates in diabetic retinopathy. The lesions are generally seen easily by most observers, and the evaluation of the fundus is based on the Gestalt of the overall appearance of the fundus, its vasculature, and frequently the changes noted by comparison with a previous retinal image. In the case of fluorescein angiograms, the situation is similar. Although specific lesions such as leakage should be detected and localized, those are relatively easy to find in the late images. The analysis of earlier images in the sequence is, nevertheless, used to generally evaluate the hemodynamic of the fundus, which may be of importance in determining treatment decisions. Although such observations may benefit from image enhancement, it is even harder to demonstrate such improvement without a clear, measurable variable (such as detection). Even for situations where the imaging evaluation task can be reduced to a detection task (such as detecting an RNFL lesion, or detection of at least a single retinal lesion in early diabetic retinopathy) the critical evaluation of image enhancement benefit is not simple due to the lack of a "ground truth." In radiology, where the image of a lesion is obtained and followed by biopsy, the nature of the observed lesion can be determined. In ophthalmology, only rarely do we have the convenience of such an immediate, independent verification of the existing lesions. In most cases, such information can only be obtained with extended followup that can eventually verify the existence of the disease noted first from a fundus image. The long period of time required for such developments make the availability of such lengthy follow-up data rare.

ENHANCED INTERPRETATION OF DIAGNOSTIC IMAGES

Hunt (13) noted that although restoration was one of the first applications of digital image processing, it has declined in importance in recent years. He attributed this to the increased complexity of image restoration systems which now require sophisticated input from the human operators to perform successfully. This reliance on human input goes against the aim of most computerized applications today. Nevertheless, the improvement of diagnostic performance with fundus images may depend on improving the human observer rather than changing the images.

A recent series of studies suggests that the performance of medical image interpreters may be improved using a different type of computerized aid (10,39). In these studies evaluation of mammography by general radiologists was shown to improve with the use of objective interpretation aids. The aids consisted of a checklist requiring the observer to provide quantitative assessment of important features in the image. A computer program merges these assessments to estimate the likelihood of a specific diagnosis. The radiologist then uses the estimate as a guide to the final decision. Performance with these aids and without image enhancement has been demonstrated to improve the classification of lesions into benign or malignant categories when the experimenter pointed out the lestions to a radiologist (10). These aids also improved performance in a more realistic task in which radiologists themselves were asked to detect and classify lesions (39).

STUDY POPULATIONS

More important for our discussion is the finding that the measured improvement is highly dependent on the selection of cases. When only the more difficult cases are evaluated, the effect of the diagnostic aids was substantially larger than when the whole population of cases was used (39). This finding has serious ramifications for the evaluation of imaging modalities in general, including enhancement. It indicates that the outcome of a comparison study of two techniques may depend on the difficulty of the cases selected for the test. Under one selection the differences in the results will be of little significance, while a different set of images may result in a highly significant difference. As a general rule, the comparison of techniques with ROC analysis will be affected by the overall level of performance. Observers who perform well with unenhanced images do not have much room for improvement with the enhanced images (25). Thus, the analysis of the diagnostic benefit of enhancement of medical images is difficult and requires careful design, which may rival the difficulty of designing new and improved enhancement techniques.

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