Current problems and perspectives on colour in medical imaging

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Abstract

Medical practitioners are today increasingly likely to make clinical judgements based on looking at an image on a display rather than direct viewing of the subject. Medical imaging has also been moving away from exclusively grayscale modalities towards increasing use of colour. The importance of accurate calibration and reproducible image capture and display has become more apparent, but standards and best practices in this field are still in development. Since 2013, the International Color Consortium has engaged with the medical imaging community to help understand the particular problems encountered and to help develop solutions. Currently the ICC Medical Imaging Working Group is working on a wide range of topics including digital microscopy, medical displays, ophthalmology, medical photography, multispectral imaging, petri dish imaging, dermatology, skin colour measurement, and 3-D imaging for surgery. In this overview, the problems in each of these areas are summarised and the current activity is described.

Introduction

The general trend in medical imaging today is to replace direct viewing (e.g. of x-ray film, microscope slide, photographic print...) with viewing of digital images on a display. The medical practitioner is increasingly likely to view images without access to an 'original', and often remotely. In primary (diagnostic) reading environments high-performance displays are used with the potential for accurate calibration, but practitioners increasingly rely on mobile devices such as smartphones and tablets to review and even possibly diagnose medical conditions.

Colour images, whether false-colour or true-colour, can provide additional information of potential diagnostic value. The range of medical imaging modalities where colour calibration and colour accuracy are considered important is very wide, ranging from in-vitro diagnostics, microscopy, dermatology, video endoscopy, ophthalmology and in each of these areas imaging modalities are in development and in most cases yet to undergo standardisation. Some common themes of these imaging modalities are the need for consistent and accurate colour calibration, and exchange of colour images in an open, consistent and interoperable way. In this respect previous ad hoc approaches to calibration are recognised as having serious limitations: in particular, colour appearance is arbitrary, depending on factors such as the capture device and the current display state. In the past, colour has not been a priority in medical imaging as most images of diagnostic interest have been grayscale. Although well-defined methods exist for grayscale calibration [1], the methods for colour calibration across capture and display are lacking in standards and associated tolerances. Medical devices require regulatory approval and must demonstrate both safety and efficacy, and the lack of standards is a barrier to wider use of colour in medical imaging.

The DICOM standard for medical images provides a path for colour interpretation in the medical image workflow by recommending ICC profiles for all colour images, although in practice this is not always followed and an sRGB assumption is a common fall-back. Although the evidence for a direct effect of colour accuracy on diagnostic outcomes is limited, practitioners acknowledge that ad hoc rendering and interpretation of colour images leads to inconsistency.

Colour modes in medical imaging

Medical image colour modes include grayscale, false-colour and true-colour.

Grayscale images arise from a mapping of intensities (e.g. from X-ray, computerized tomography (CT), nuclear Magnetic Resonance Imaging (nMRI) scanners) to tonal levels in an image. In some cases, 2-D images represent planes of information that can be combined into a 3-D representation of the body or body part.

A key requirement for grayscale medical images is to support feature discrimination, both by visual inspection and by image processing. Greyscale medical images are commonly acquired by systems that record radiometric quantities and map them linearly to values within the quantization range, and feature discrimination is supported by ensuring that the recorded grayscale steps are presented in a way that is visually uniform. This is achieved by ensuring that the display used to view the images is calibrated to the Gray Scale Display Function (GSDF) [2], based on work by Barten [3, 4].

Grayscale images are often modified by addition of colour to aid in discrimination of features. Such false-colour images include pseudo-colour (in which intensity levels are mapped continuously to different colours), density slicing (where the image features are mapped categorically to a smaller set of discrete colours) and chloropleths, (where features are coloured in a way that is proportional to a particular statistical variable). In medical imaging, the term pseudo-colour is commonly used to imply any type of false-colour image. Mapping from intensity to colour is specified by an arbitrary transform or look-up table, and DICOM specifies a selection of colour palettes for specific applications [5] (such as PET for pseudo-colouring PET images when fused with grayscale CT images) and the use of a palette colour look-up table to transform from grayscale to pseudocolour.

Since false-colour images share the objective of supporting feature discrimination, the presentation goal is to ensure perceptual uniformity of the colour channels. By analogy to GSDF, this would imply calibration to a Color Scale Display Function (CSDF); CSDF is a work in progress, and is discussed in more detail below.

An increasing number of imaging devices used in medical imaging are based on multi-band sensor arrays rather than a single intensity channel. Trichromatic imaging devices, recording RGB signals, are common but multi-spectral and hyper-spectral devices also exist and have been shown to have value in particular applications. Such RGB images are often referred to as true-colour images, since they approximate the visual appearance of the subject rather than a completely arbitrary mapping from sensor response to colour.

One principal requirement for true-colour images is colorimetric accuracy with respect to the subject being imaged. Perhaps more so than in other applications, medical images also have a high requirement for consistency in order to be able to judge small differences in appearance between images, whether acquired by the same device at different times, or by different devices of the same subject.

Many of the current problems in colour in medical imaging can be classed as problems of calibration of image capture and display systems. Medical imaging has specific requirements that are not encountered with other imaging systems, and this paper summarises some of the work being done in this area.

Medical Imaging Working Group

Experts from both colour and medical imaging communities came together in May 2013 in a two-day Summit on Colour in Medical Imaging [6]. The meeting was organised by ICC and FDA with 27 speakers, and 250 delegates from around 30 countries. Topics included digital microscopy, endoscopy, laparoscopy, telemedicine, displays, ophthalmology, multispectral imaging, mobile devices, medical photography and standards for colour. A 'Task force' was formed at the meeting, which became the ICC Medical Imaging Working Group and experts agreed to lead work in each area. A consensus paper from the Summit has been published [7], summarising problems in each of the topics discussed.

The ICC profile format and architecture provides a solution framework for many of the current problems in medical imaging, and the primary aim of the Medical Imaging Working Group is to enable and promote the correct and effective use of ICC colour management for medical imaging. Specifically the group will:

1. Identify issues with the implementation and use of colour management for medical imaging.
2. Establish and maintain liaison relationships with the appropriate medical imaging standards development organizations, e.g. DICOM, AAPM, ACR, IEC and ISO.
3. Prepare white papers and other educational materials, and promotion activities to guide developers and users in the appropriate application of colour management to medical imaging.
4. When necessary, propose new ICC specifications or revisions to existing ICC (and other) specifications to address the needs of the medical imaging community.
5. Promote the use of ICC colour management in medical imaging. [8]

A MIWG web site has been established [9], which provides a summary of activities including recordings, presentations and minutes from teleconferences and face-to-face meetings. Individual MIWG web pages provide a summary of each of the topics currently being progressed.

MIWG has broad participation from ICC members and non-members, and each work area is led by an expert in that field. As with all ICC working groups, members agree to comply with ISO guidelines on intellectual property. The group holds monthly teleconferences and three face-to-face meetings each year.

Current issues being addressed by MIWG

The current set of issues being addressed within MIWG is listed on the MWIG web site [9]. At the time of writing it includes:

- Calibration slide for histopathology
- Medical RGB color space - mRGB / dRGB
- Color eye model
- Best practices for digital color photography in medicine
- Colour support for mobile devices
- Framework for multispectral imaging
- Petri plate calibration
- Imaging and reproduction of skin

Within these areas of activity, microscopy and display calibration have most contributions to date, and are outlined below. Other topics are summarised very briefly.

Whole-slide imaging.

In digital microscopy, slides are imaged for analysis and display. Histopathology samples may be stained with coloured dyes that enhance tissue components, providing biomarkers that indicate conditions such as diseased cells. Such coloured elements are used by pathologists to identify the presence (or absence) of disease. The colours present in the image depend on many factors, including the microscope optics, imaging sensors and sample illumination. Within a single system, different settings can lead to significant variation in image appearance. [10] Owing to a lack of calibration, different microscopes generate very different images from the same slide, leading to potential inconsistency in diagnosis and difficulty in automating some parts of the diagnostic process. MIWG members are evaluating different assessment and calibration methods: in one method a slide containing a selection of test colours is visually compared with a display of the acquired image [11, 12], while in another method a calibration assessment slide incorporates pathology stains on a biopolymer support [13]. The stained biopolymer calibration slide (Figure 1) incorporates a total of 60 stains and stain combinations, based on Eosin, haematoxylin, DAB, tartrazine, picric acid, Van Gieson, PAS, Light Green SF, Orange G, Aniline Blue, Neutral Red and Crystal Scarlet stains. It was found that the absorption spectra of stain combinations could be modelled by linear additivity, and there was good agreement between the measured absorption spectra of stained tissue and the stained biopolymer. It was also found that Eosin was prone to fading on exposure to light, and treatment with DABCO had the effect of stabilising the treated Eosin patches and also providing a fading reference when compared to untreated patches. Preliminary results indicate a significant improvement in inter-instrument agreement when this procedure is used [13], and a manufacturer for the calibration slide is being sought.

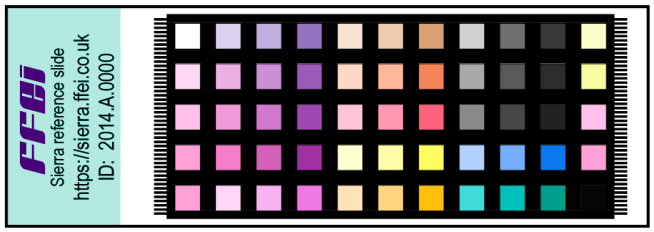

Figure 1 Sierra calibration slide

A third promising method uses a linear variable filter to characterise the combination of light source and sensor sensitivities [14]. These are then combined with known spectra from stained specimens to construct an ICC Profile for the digital microscope. One commercially available solution uses a similar approach where a set of very small dichroic filters are used to characterise the sensor.

Medical displays.

Since grayscale radiological images were the primary use case in medical imaging until recently, medical displays are calibrated using the Grayscale Display Function (GSDF), which optimises the discriminability of incremental drive values at a range of different display peak luminance levels. Grayscale displays for primary diagnosis often have peak luminance levels of 400-600 cd/m2, and for clinical review 250-450 cd/m2 [15]. Since different peak luminance levels result in different GSDF curves, a media-relative calibration may not be appropriate and the DICOM specification [1] defines how medical displays should be calibrated to different luminance levels. IEC 62563-1:2009 specifies methods and tools for grayscale calibration [16]. AAPM Task Group 196 is currently drafting a consensus report on 'Gray tracking in medical color displays'.

With some exceptions, colour displays do not normally reach the luminance levels of diagnostic grayscale displays, and are more likely to have a luminance in the range of the clinical review display.

Some work has been done that analyzes the importance of calibration accuracy in diagnosis [17, 18, 19], but currently there is no agreed standard for colour calibration. For pseudo-colour images, it is considered that the display should, analogously to the grayscale display, present incremental RGB drive values such that they are perceptually uniform. True-colour images are most commonly encoded as sRGB, and the display requirement is to ensure accuracy relative to the sRGB encoding in a media-relative sense, allowing for the differences in peak luminances of the displays. In some cases an embedded ICC profile defines a source colorimetry different from sRGB. The DICOM specification requires that all colour images include an embedded ICC profile.

These three use cases for colour images imply three different calibration possibilities: for pseudo-colour images, a colour scale display function has been proposed [20]; for sRGB images it is sufficient to calibrate the display directly to the sRGB standard; while for other true-colour images the embedded profile can be used to convert to the display calibration state. Only the last of these cases requires the use of ICC colour management. However, in many situations images from different sources are displayed simultaneously, and the display then needs to support multiple calibration states.

For pseudo-colour images, current work is focusing on the possibility of extending the GSDF concept of uniform discriminable steps into 3-dimensional colour space, referred to as Color Scale Display Function (CSDF). [20] The CSDF model would require a 3-D look-up table to ensure that RGB values represent equal visual spacing, defined as equal CIEDE2000 colour differences. For true-colour images a DICOM RGB (dRGB) colour space has been proposed, with a peak luminance range of 250-450 cd/m2 and a white point chromaticity of D65, but with no specified chromaticities for the primaries.

Guidelines have been developed for display calibration for medical imaging using ICC colour management [21] based on an empirical study, which include recommendations for a 10-bit display pipeline and a 3-D lut with a minimum of 33 grid points in each dimension.

Colour eye model

Fundus cameras produce widely varying images of the same retina, as can be seen in the example in Figure 2. Although previous work has addressed the problem of consistency between different systems [22, 23], until now there has been no method of calibrating such cameras in a way that leads to accurate or consistent colour images.

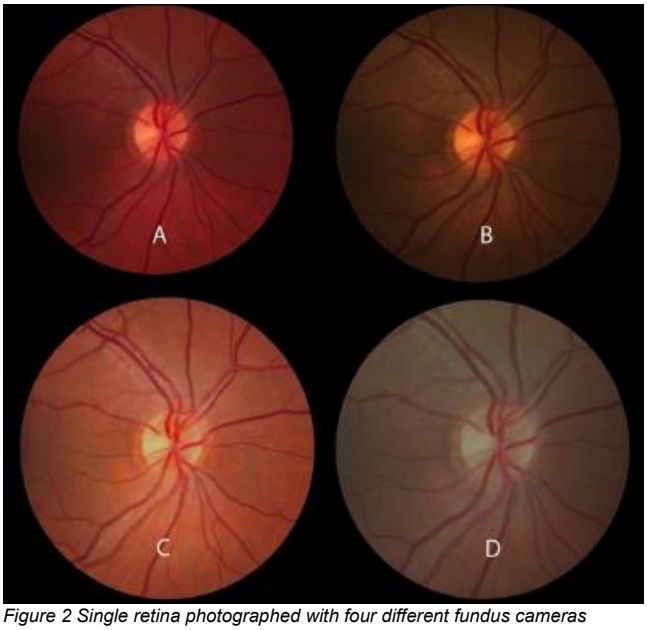

Figure 2 Single retina photographed with four different fundus cameras

A miniature, flexible ColorChecker-type test chart has been developed that can be inserted into a model eye and used to calibrate the camera (Figure 3). The target is inserted in to a 'model eye' and captured at normal exposure once the alignment working distance and focus have been established. This approach is currently being trialled at multiple sites, and based on preliminary phases custom colour patches with optimal reflectances for fundus imaging are being developed and methods of producing the target tested. The imaging protocol is also being modified for angle of view and illumination, and software implementation strategies are being considered. [24]

Figure 3 Phase II Fundus camera calibration target

Best practices for digital photography in medicine

Medical photography is used to record aspects of a patient's appearance such as dermatological conditions, wound healing etc. In some cases colour accuracy is considered important, and the deviations occurring in a colour capture workflow have been summarised. [25] The goal of this activity is to provide guidelines

to practitioners on procedures which can minimise colour errors on different cameras and lighting conditions. The intent is to base the guidelines around existing best practice in professional photography, including the use of RAW image data and suitable methods to convert this data to device-independent colour spaces.

Mobile devices

While high-end calibrated displays are used in primary reading environments, medical practitioners also need to view images in other situations, using mobile devices such as tablets and smartphones. The colour management framework on such systems is often weak, and methods of supporting colour calibration on such devices are needed.

Petri plate imaging

Microbiology labs are increasingly automating the process of assessing petri plates through scanning and image processing [26, 27]. This can significantly increase productivity and reduce resources, but the challenge is to provide equivalent information to manual plate reading, which may include additional channels such as smell and 3D vision. Direct visual reading does not suffer from the distortions of the imaging chain, including the variable accuracy of the capture and display systems used. Imaging systems need to include different lighting conditions to maximise the information provided by the scan, as illustrated in Figure 4.

Progress is being made in this area [28] on defining a measurement protocol for spectral characterization, a colorimetric image quality assessment method, and a unified display management framework for colorimetric and multispectral images [29].

Imaging and reproduction of skin

Activity is being directed towards understanding the challenges in measurement and reproduction of normal and diseased human skin for diagnostic purposes and for the building of tissue prostheses [30]. Methods of estimating skin reflectance from camera images are being developed [31] and a database of skin images and associated spectral reflectance data is being built [32].

Conclusions

Accuracy and consistency of calibration for medical imaging is now receiving the attention it deserves, and work is taking place in many different fields. Common to most of these activities is the need for interoperability, consistent cross-media reproduction, standards and compliance tools. The ICC colour management framework provides a basis for addressing many of these problems, and in particular enables vendors and users to add images and devices to a medical imaging workflow with minimal effort. The ICC Medical Imaging Working Group is an open forum for discussion and exchange of ideas, governed by ISO guidelines on intellectual property. Experts are warmly encouraged to participate in MIWG, and more information can be found at the MIWG web site [9].

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