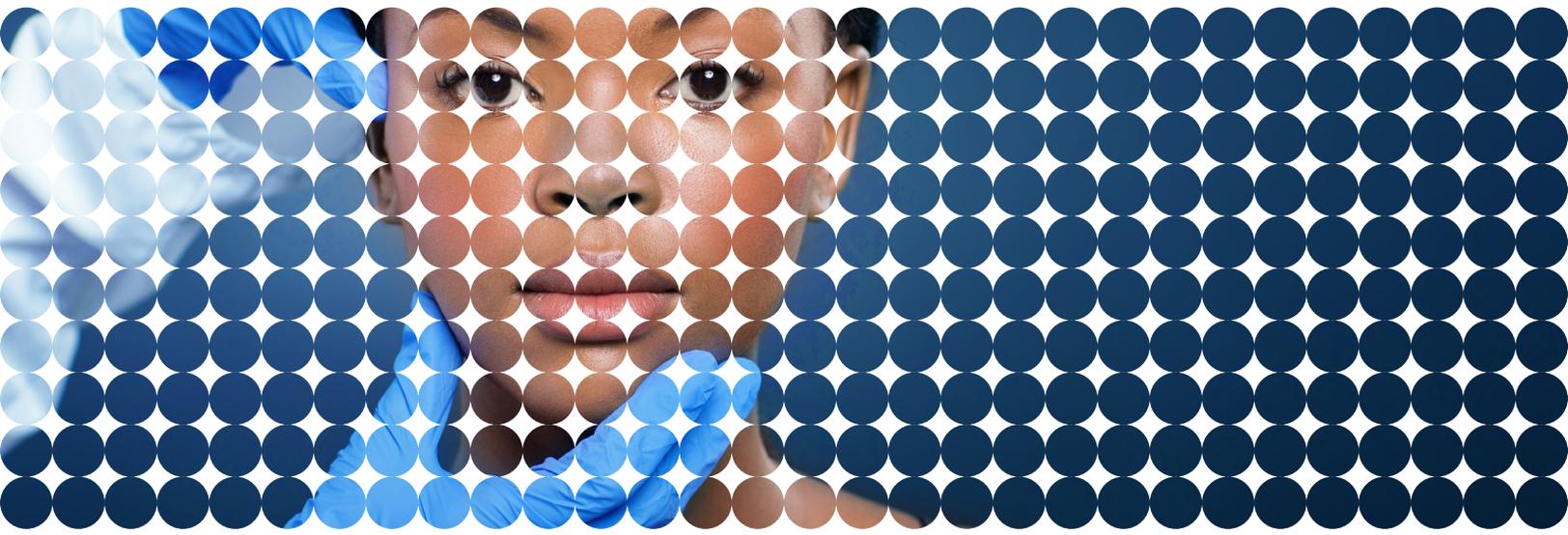




CHILTERN
Designed Around You®



A Picture is Worth a Thousand Words: Clinical Photography in Dermatology Trials

Niamh Bresnihan
Chiltern Project Director

Introduction

Skin disease affects between 30% and 70% of the world's population. Seen in people of all ages and across all countries and cultures, the impact ranges from mild and temporary to serious and chronic [1]. There is a huge global market for drugs to treat dermatological conditions, worth around \$24.1 billion in 2014 [2]. Companies that want to be able to tap into this dermatology market need to analyze the safety and efficacy of their drugs in clinical trials, utilizing a variety of instrumental methods with clinical photography as a vital tool.

Photography In Clinical Trials

In clinical trials, clinical photography is used to track the rate and extent of visible changes over the length of the study. These include changes in the size and color of lesions, skin color measurement (e.g., erythema or pigmentation), or changes in texture, such as inflammation and scaling. These criteria can be combined with patient and clinician reported outcomes, as well as other safety and efficacy clinical endpoints, to provide data for progression of the clinical trials, or ultimately the submission for marketing approval. Photographs may also be used for marketing purposes, if the patient provides consent.

There are a number of factors that need to be taken into account when preparing for dermatology clinical trials, all of which will help to ensure that the quality of the data is as high as possible:

- Trained technician staff
- Patient preparation and impact of color
- Choosing the camera and setup
 - Equipment logistics
 - Lighting and positioning
 - Location
- Photography techniques

Patients have to provide consent for clinical imaging, separate to study consent, allowing study involvement without photography if preferred. As patients with disfiguring skin disorders may have significant issues with confidence and be anxious about their appearance, their initial experience at the trial site, along with reassurance about security and privacy of the images, is therefore vital. To ensure this, photographs taken during clinical trials need secure storage and transmission for analysis. This can be via a secure website or carried on password-protected DVDs or portable hard drives.

Dermatology studies can be long and time-consuming, which is a particular issue for people who are at school or college, or who are working. Ensuring that they do not have to attend too often, feel 'looked after', and gain something in the way of care or education will help with retention.

Patient Preparation and Impact of Color

In order to get the most data from the image, it's important that there is as little as possible that could interfere with the photography process. This includes cleansing to reduce shininess and clean off any makeup; however, redness caused by washing needs to be allowed to return to normal. Fringes (bangs) and long hair should be pulled back from the face [3], and jewelry removed to avoid shadows or reflections.

Contents

2	Introduction
3	Finding the Location
4	Lighting and Positioning
5	A Picture is Worth a Thousand Words

Color plays an important role in the analysis of digital images in dermatology clinical trials, and can be affected by colors in the skin, clothing and environment [4]. Skin color is determined by patient genetics and ethnic origin. Lighter-colored skin can lead to flash 'blow-out', whereas darker skin will absorb light. Changes in skin color through tanning may make it harder to compare results in a trial carried out over a long period.

Clothing colors, especially near to the area being photographed, will have an impact. Dark clothing will absorb the flash, and light colors throw it back, affecting the color saturation and brightness of the photo. Wherever possible, clothing should be removed near the area to be photographed. If this isn't feasible, patients can wear standard clothing, or cover clothing with neutral drapes.

The colors of the furniture and walls should be as neutral as possible, the photographs taken against a neutral background, for example one provided by the equipment supplier.

Finding the Location

The trial site for a dermatology study must include a room that is large enough for the equipment, staff and patient. While the camera itself may not be large, the set up may also require a chair for the subject, a table for the camera, lighting stands, a neutral background, and any patient placement devices and measurement aids. The light levels in the room must be able to be standardized for all patients and all visits throughout the entire study, for example with no natural light, or blackout curtains or blinds [3]. The site must also have space to store the equipment for the duration of the study.

Choosing the Camera and Setup

The cameras used in photographing skin lesions may be standard digital devices, or special-purpose imaging systems. Specialist systems range from handheld devices with cone-shaped attachments and built-in illumination to standardize the light levels, distance and area of skin photographed, through dedicated facial imaging devices to 3-D systems that track changes in skin morphology during treatment [3]. For example, Quantificare's 3D LifeViz® Mini system is an all-in-one 3D imaging system. Its small size and portability combined with dual beam pointers to fix the distance means that companies can procure superior quality and reproducible images and be more flexible about site choice [5].

Equipment Logistics

The equipment choices will depend largely on the data collection requirements of the trial; however, the size of the rooms available for patient assessments and the space required for storing the equipment between patient visits may also be influences.



Figure 1: Cross-polarized or nonpolarized (standard) lighting modes of specialized lighting systems can visualize skin texture and color.

The same camera make and model and the same lighting setup needs to remain constant throughout the study, in all clinical trial sites, to maintain image color and quality consistency. Because of this, pharmaceutical companies often use specialist suppliers who can ship equipment directly to the site, carry out photography skills training and validation, and retrieve the apparatus at the end of the study.

Lighting and Positioning

The simplest approach to lighting is by using camera-mounted flash systems, with through-the-lens metering systems that can monitor light levels. Adjustable studio lighting, whether as part of a unit that includes the lights and camera, or as separate lights that can be positioned as needed, can be an option when a larger space is available, and may be more flexible [3]. Specialist lighting systems can be useful to pick out specific features, for example the VEOS dermatoscope uses either cross-polarized or nonpolarized (standard) lighting modes to visualize skin texture and color. These variables are being used as outcomes in dermatology clinical trials [6].

Once the setup is complete, the positioning of all the equipment, the furniture, and even the patient needs to be recorded, so that it can be repeated at every visit to create a reproducible set of images. This may be as simple as tape on the floor to mark the position of the chair, table, lighting stands and backdrop, with additional marks on the tabletop indicating where to place the camera. Imaging booths are a higher tech, though higher cost, solution. An example is Canfield's Visia-CR turnkey facial imaging system. This provides close up photography using a high-resolution camera, headrest and chin cup, xenon flash based lighting, and multi-spectral filtering options. This system can provide standardized images of spots and wrinkles, with analysis of skin texture, color, color evenness and porphyrin production [7].

Training and Photography Techniques

Photographs used in clinical trials must be clear, consistent, and repeatable to ensure the recorded changes are reflecting baseline and treatment results rather than differences in the process (e.g., the image resolution or color saturation). This relies on training that includes how to set up and use the equipment and how to position the patient.

Training can be in person or online and is validated through assessment of test photographs continued throughout the clinical trial period to maintain standards. Online training ideally should be backed up with other materials and guidance.

Although the training process provide sufficient background and instructions for carrying out the imaging part of the study, using sites and staff with previous experience in photography and the specific type of equipment used can make the setup of the trial easier and give the trial sponsor greater confidence in the outcomes. Basically, using more experienced staff will help ensure the quality of the data is as high as possible.

For studies that focus on small areas of skin rather than a full face, it is critical to use the same magnification. Something like a pair of diagonally-placed tattoos can be used to define an area for imaging, allowing photographs to be taken at fixed focus, distance, and exposure [8]. If possible, an existing mark such as a mole or scar could also be used as a marker.



Figure 2: Special-purpose imaging systems range from handheld 2D devices with cone-shaped attachments and built-in illumination to standardized the light levels, distance, and area of skin photographed, through dedicated facial imaging devices to 3-D systems that track changes in skin morphology during treatment.

A Picture is Worth a Thousand Words

Images are an important, supportive, part of the data resulting from dermatology clinical trials. Although the value of photography is without question, it is not a substitute for the dynamic evaluation of a patient in the clinical setting by a trained professional. For example, lesion counting for acne is not as accurate via photography alone. Photography corroborates/augments the clinical trial and patient evaluation process. Together with other measurements of clinical parameters, images help to create a package to underwrite submission for approval and support post-approval marketing efforts.

In addition to choosing the right site, getting the right equipment in place, and ensuring that lighting and other environmental criteria are kept standardized, you should also make sure the patient has a good experience. Accomplishing all of that will ensure the imaging data is as robust and reproducible as possible.

References

1. Hay, R.J., et al., The Global Burden of Skin Disease in 2010: An Analysis of the Prevalence and Impact of Skin Conditions. *Journal of Investigative Dermatology*, 2014. 134: p. 1527–1534.
2. Dermatological Drugs Market Forecast 2014-2024: Future Prospects for Leading Companies. Visiongain. 15 April 2014. Available from: <https://www.visiongain.com/Report/1242/Dermatological-Drugs-Market-Forecast-2014-2024>.
3. Witmer, W.K. and P.J. Lebovitz, Clinical photography in the dermatology practice. *Semin Cutan Med Surg*, 2012. 31(3): p. 191-9.
4. Lindner, A. and S. Winkler. What impacts skin color in digital photos? in *Color Imaging XIX: Displaying, Processing, Hardcopy, and Applications*. 2014. San Francisco, California, USA: Proc. SPIE
5. 3D LifeViz II. Qunaticare. Created: 2011. Last Accessed: 1 June 2015; Available from: http://www.quantificare.com/index.php?option=com_content&view=article&id=7&Itemid=73.
6. François, G., et al., Quantification of Facial Pores Using Image Analysis. *Cosmetic Dermatology*, 2009. 22(9): p. 457-463.
7. Visia-CR. Canfield. Last Accessed: 28 May 2015; Available from: <http://www.canfieldsci.com/imaging-systems/visia-cr/>.
8. Dhurat, R., et al., A randomized evaluator blinded study of effect of microneedling in androgenetic alopecia: a pilot study. *Int J Trichology*, 2013. 5(1): p. 6-11.

SITE, ENVIRONMENT AND EQUIPMENT REQUIREMENTS:

- Controllable lighting
- Plain, neutral backgrounds
- Specialist equipment, tailored to the study and standardized across sites

TRAINING ESSENTIALS:

- Training to ensure clear and consistent images
- Support from additional materials and guidance

THE PATIENTS NEED TO:

- Provide signed photo consent forms
- Wear suitable-colored clothing that can be removed easily
- Clean skin, tie hair back and remove jewelry



CHILTERN
Designed Around You®

2528 Independence Blvd., Suite 101
Wilmington, NC 28412
USA
+1 910 338 4760

171 Bath Road
Slough, Berkshire SL 14AA
England, UK
+44 (0) 1753 512 000

lets.talk@chiltern.com
www.chiltern.com