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The microcirculation image quality score: Development and preliminary evaluation of a proposed approach to grading quality of image acquisition for bedside videomicroscopy $\stackrel{\sim}{\succ}$

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ABSTRACT

Purpose: Side-stream dark-field microscopy is currently used to directly visualize sublingual microcirculation at the bedside. Our experience has found inherent technical challenges in the image acquisition process. This article presents and assesses a quality assurance method to rate image acquisition quality before analysis. *Materials and Methods:* We identified 6 common image capture and analysis problem areas in sublingual side-stream dark-field videos: illumination, duration, focus, content, stability, and pressure. We created the

"Microcirculation Image Quality Score" by assigning a score of optimal (0 points), suboptimal but acceptable (1 point), or unacceptable (10 points) to each category (for further details, go to http://www.MicroscanAnalysis. blogspot.com). We evaluated 59 videos from a convenience sample of 34 unselected, noncritically ill emergency department patients to create a test set. Two raters, blinded to each other, implemented the score. Any video with a cumulative score of 10 or higher (range, 0-60) was considered unacceptable for further analysis.

Results: We created the Microcirculation Image Quality Score and applied it to 59 videos. For this particular set of 59 videos, the mean (SD) passing quality score was 1.68 (0.90), and the mean (SD) failing quality score was 15.74 (6.19), with 27 of 59 passing the quality score less than 10. Highest failure occurred from pressure artifact. The interrater agreement for acceptability was assessed using Cohen κ for each category: illumination ($\kappa = 1.0$), duration ($\kappa = 1.0$), focus ($\kappa = 0.91$), content ($\kappa = 0.76$), stability ($\kappa = 0.71$), and pressure ($\kappa = 0.82$) and overall pass-fail rates (score >10) ($\kappa = 0.66$).

Conclusion: Our Microcirculation Image Quality Score addresses many of the common areas where video quality can degrade. The criteria introduced are an objective way to assess the quality of image acquisition, with the goal of selecting videos of adequate quality for analysis. The interrater reliability results in our preliminary study suggest that the Microcirculation Image Quality Score is reasonably repeatable between reviewers. Further assessment is warranted.

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1. Introduction

Microcirculatory blood flow, the blood flow through the capillaries where oxygen exchange occurs, is an important part of the pathophysiology of a number of disease processes. Recent technological advances using side-stream dark-field (SDF) videomicroscopy now allow for the direct visualization of the microcirculation in real time at the bedside [1]. The capillary bed of the sublingual surface is used as a feasible, readily accessible, and representative location to visualize the microcirculatory flow. To quantify the flow, measurements in 3 main areas are proposed as core metrics: vessel densities, perfusion indices, and heterogeneity indices [2]. Using these assessments, a number of research studies have successfully quantified the imaged vessel density and flow rate captured in the videos and demonstrated an association between the quantified microcirculatory parameters with measures of physiology, morbidity, and mortality [2-8].

However, the bedside device presents practical challenges inherent to the clinical environment. The video microscope is hand held by

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the user. Focus and illumination are adjusted manually while the operator views a video monitor. The user must hold the tip of the microscope steady with less than approximately 0.1 mm/s of lateral movement while not applying too much pressure to occlude flow. Similarly, the patient must remain still and cooperative. Captured videos are typically edited and analyzed offline. During offline preprocessing, the investigator reviews minutes of video to select a 5- to 20-second segment that is representative of the vessel density and flow and is suitable for further analysis. Representative segments are chosen to avoid video that samples a capillary bed that is out of the plane of focus, or that drifts to a region with predominantly looped vessels, or at a time when the microscope tip exerts too much or uneven pressure on the mucosa.

To date, the description of the microcirculation in the medical literature has largely focused on the flow and density characteristics. Although there have been a few preliminary efforts to assess the quality of the video acquisition, no systematic criteria are routinely used. For example, Sallisalmi et al [9] evaluated SDF videos for technical quality, and the roundtable consensus report on evaluating the microcirculation did suggest 5 key points for optimizing image quality (sample 5 sites per organ, avoid pressure artifact, eliminate secretions, maintain adequate focus and contrast adjustment, and obtain a high-quality recording) [2]. We believe that these criteria may be expanded on and that a set of criteria that define characteristics that verify which acquired video is suitable for analysis and provide a systematic and quantitative approach would be useful. Based on our experience, we identified 6 common areas of image degradation: focus (blurred images), illumination (too light or too dark), content (saliva bubbles or vessels in tight loops), duration (video is too short in time), movement (jitter or translation), and pressure (iatrogenic occlusion of vessel flow due to the probe tip). We propose that one should systematically assess these different domains to determine the quality of the acquired image, before moving on to score the content of the image. Furthermore, one should not analyze poor-quality images because this may generate spurious data (eg, if during image acquisition, the investigator pushes too hard on the microvasculature, it will give an image of occluded flow).

To address the need for a systematic approach to assess the quality of image acquisition, we propose the Microcirculation Quality Score. Accordingly, the aim of this work is to describe a system for researchers to quantify the quality of sublingual SDF videos and to preliminarily assess interrate reproducibility for the system. These scoring metrics are proposed to provide a methodology to identify videos that are unacceptable for analysis and to characterize the deficiencies.

Table 1

Quality scoring metrics

Good (0) Acceptable (1) Unacceptable (10) Illumination: brightness and contrast of Even illumination across the entire field The video borders on being too dark or The video is oversaturated/too bright or too the video of view. Contrast sufficient to see small bright to distinguish vessels from tissue but dark to make out analyzable features. vessels against a background of tissue the vessels are still identifiable Insufficient contrast to resolve flow rate Duration: number of frames in the video Analyzable video segment is ≥ 5 s long Analyzable video segment is 3-5 s Analyzable video segment is <3 s (<90 (between 90 and 150 frames) clip and how it represents the actual (>150 frames) frames) pathology Good focus for all vessels (small and <1/2 field of view is out of focus or edges of Video is completely out of focus such that no Focus: image sharpness in region of interest large) in the entire field of view. Plasma the vessels are slightly out of focus. small vessels can be seen. gaps and red blood cells are visible. Content: determination of the types of Video is free of occlusions. Good Video may have a few artifacts. Acceptable Most of the field of view has occluding vessels and/or presence of occluding distribution of large and small vessels. artifacts such as saliva or bubbles. More than distribution of large and small vessels. artifacts in the image. If the video Less than 30% of the vessels are looped About 30% to 50% of the vessels are looped. 50% of the vessels are looped upon presents overall pathology upon themselves. themselves Stability: frame motion that can be Movement is within 1/4 of the field of Movement is within 1/2 of the field of view. Movement is greater than 1/2 of the field of adequately stabilized without motion view. No motion blur view and/or motion blur in frame. No motion blur blur Pressure: iatrogenic mechanical pressure Flow is constant throughout the entire Signs of pressure (localized sluggish flow in Obvious pressure artifacts associated with causing misrepresentation of flow movie. No obvious signs of artificially a specific large vessels), but flow appears to probe movement, and/or flow that starts and

sluggish or stopped flow. Good flow in

the largest vessels

2. Materials and methods

2.1. Description of the microcirculation image quality score

Six categories were used for scoring each video clip. Each video was given a score of 0, 1, or 10 for each category (Table 1). The total Microcirculation Image Quality Score is defined as the sum of the scores for all the individual categories. An individual score of 0 indicates that the video was "optimal" and that there were no problems for a specific category. A score of 1 indicates that capture was "suboptimal but acceptable" and adequate for analysis in a specific category. A score of 10 indicates that the video was "unacceptable" for a particular category. We chose "10" as unacceptable to create a system where if any component of the metric is unacceptable, the video automatically fails quality scoring. With this system, several suboptimal scores do not add up to the failure score of 10. When multiple video clips are available for a given patient, the total Microcirculation Image Quality Score enables the selection of the videos with the highest overall quality. The difference between a 0 (optimal) and 1 (suboptimal but useable) in any category is of less consequence than giving a score of 10 (unacceptable). We submit that videos with scores of 0 and 1 are still useable, whereas videos with a score of 10 in any category are not analyzable because they may yield spurious findings. For this reason, we calculated interrater agreement for unacceptable scores for each category, ignoring variations between optimal and suboptimal but acceptable scores.

2.2. Category specific definitions

be unimpeded based on good flow in most

large vessels

The following 6 categories were used for scoring the video clips, such as illumination, duration, focus, content, stability, and pressure, and the description of each is outlined in Table 1.

Illumination is based on the overall image luminance. When an image is overilluminated or underilluminated, it will appear too bright or dark. The illumination is adjusted by the operator. Brightness and contrast may adjusted during the analysis process, but if the intensity values of the video are skewed too far in either direction, image data are lost. Underillumination problems may be corrected to some degree with postacquisition processing through intensity histogram adjustments and other image processing techniques, but in some cases, the data are too dark to resolve blood flow from video noise. In videos with overilluminated areas, vessels may be washed out and no longer visible, something that is not easily recovered with postprocessing. Thus, there is a trade-off between noise (too dark) and saturation (too bright) whereby the right balance is preferable,

stops, reversal of flow. Poor or changing flow

in larger venules

but one should err on the side of underillumination if a proper balance may not be achieved.

The scores are assigned as follows: optimal (0), even illumination across the entire field of view with sufficient contrast to see small vessels against a background of tissue; acceptable (1), the video borders on being too dark or bright to distinguish vessels from tissue but the vessels are still identifiable, and fast moving flow is distinguished from video noise; and unacceptable (10), the video is oversaturated/too bright or too dark to make out analyzable features, with insufficient contrast to resolve flow from video noise (Table 1).

Duration is a function of the length of the video clip. Videos are clipped from larger segments to help reduce the influence of other degrading factors. A minimum number of video frames are required to accurately evaluate the flow velocities. Current literature indicates that video segments are typically between 5 and 20 seconds; however, this threshold is used for visual inspections of general density and flow [2,10]. With software assisting the analysis and through the use of video loops, based on our experience, we have judged that videos longer than 5 seconds (150 frames) are optimal (score = 0), those between 3 to 5 seconds (90-150 frames) are acceptable (score = 1), and anything of shorter duration less than 3 seconds fails (score = 10).

Focus is a measure of image sharpness, which is apparent along the high-contrast edges of the small vessels (<20 μ m). Individual red blood cell outlines are identifiable when these small vessels are in optimal focus. Out-of-focus vessels appear to have larger diameters, which falsely decrease density measurements. Successful flow analysis depends on the ability to clearly identify the movement of blood cells and discriminate the borders of individual vessels. For the Microcirculation Image Quality Score, we assigned scores based on the following: optimal (0), there is detailed focus of all vessels (small and large) in the entire field of view, and generally, if one can see individual plasma gaps or red blood cells, there is good focus; acceptable (1), less than 1/2 field of view is out of focus or edges of the vessels are slightly out of focus; and unacceptable (10), the video is completely out of focus such that no small vessels are seen.

Content examines image artifacts and vessel structure. In sublingual SDF images, artifacts can include bubbles and cloudy or bloody saliva, which may partially occlude the view of vessels or create a haze over the field of view. Looped vessel structures, usually located on the tongue, cheek, frenula, or plica sublingua, are difficult to measure flow and may not provide prognostic information. Looped vessels are defined as small-diameter ($< 20 \,\mu m$) vessels that bend back upon themselves forming short, tortuous curled structures. Fig. 1 shows an example of an unacceptable proportion of looped vessels in the field of view. For the Microcirculation Image Quality Score, the scores are based on the following: optimal (0), the video is free of artifacts, and there is a good distribution of large and small vessels with less than approximately 30% of the vessels looped upon themselves; acceptable (1), the video has at worst only a few small artifacts, there are at least some small vessels present, less than approximately 50% of the vessels in the image are looped upon themselves, and less than approximately 30% of the field of view is occluded by saliva; and unacceptable (10), the video has debilitating artifacts such as saliva or bubbles and/or more than 50% of the vessels are looped upon themselves.

Stability of the image is a measure of the overall image movement. Sublingual vasculature forms a nonrigid 3-dimensional structure. Side-stream dark-field images are 2-dimensional projections of the vessels in the field of view. Lateral image motion may often be corrected using automated image stabilization, but varying probe angle or pressure may cause vessel motion that is not correctable. Sublingual mucosa serves as a pivot point for the microscope lens (tip). Motion of the patient's head, jaw, or tongue



Fig. 1. Looped vessel structures. White arrows mark notable looped vessels. Looped vessels are defined as small vessels that bend back on themselves, forming short, tortuous, curled structures. The quality is unacceptable if more than half of the vessels in the field of view are looped. Looped vessels often appear in a repeating pattern.

can frustrate stable contact with the mucosa. Motion about the pivot point introduces motion parallax in the images that is not easily stabilized. If steady contact with the mucosa is not maintained and frame-to-frame movement is excessive, the video frame is blurred, adding systematic errors to blood flow analysis. For the Microcirculation Image Quality Score, the scores are based on the following: good (0), movement is within one fourth of the distance to the edge of the field of view with no motion blurring; acceptable (1), movement is within one half of the distance to the edge of the field of view with no motion blurring; and unacceptable (10), movement is greater than one half of the distance to the edge of the field of view and/or image has motion blur.

Pressure is an artifact caused by pressing too hard with the probe tip or by holding the tip at too steep an angle to the mucosal surface. causing the blood flow to slow, stop, or reverse direction. Although contact is needed to focus and stabilize the image, too much pressure will collapse small and large vessels, resulting in falsely sluggish or stopped flow caused by the iatrogenic mechanical pressure. Following the consensus guideline for determining pressure artifact [2], larger vessels (especially thin walled veins and venules) are used as "indicator vessels" because they are more sensitive to pressure. If there is good flow in the large vessels, significant pressure artifact is judged absent. Pressure is judged to be present if there are significant changes in flow rate of any large vessels during the course of the video clip, including flow that reverses direction, or if no blood flows in filled venules. For the Microcirculation Image Quality Score, the scores are based on the following: optimal (0), flow is constant throughout the entire movie, no obvious signs of artificially sluggish or stopped flow, and good flow in the large venules; acceptable (1), shows some ambiguous signs of pressure, such as intermittent sluggish flow in one large venule, but flow surrounding that vessel appears unimpeded; unacceptable (10), obvious pressure artifacts associated with probe movement, and/or flow that starts and stops, reversal of flow, poor or impeded flow in larger venules. If any large vessel in the field of view exhibits a pressure artifact, then the entire video will fail and receive a pressure score of 10.

We chose the domains of interest based on a combination of prior literature [2,9,11] and our experience. We wish to note at this point that this classification system is proposed as a starting point and that perhaps some of our fields should be combined or split, or maybe we omitted a field altogether whose inclusion would improve or enhance the score. Finally, perhaps the next generation of the quality scoring system will weigh categories differently or have a different scoring system for the values. Along those lines, other researchers have adopted another method for the evaluation of SDF image quality [9]. We introduce this methodology as a contribution to address an important topic and anticipate an evolution to the final product.

2.3. Study design

We performed a prospective, observational study using microcirculatory flow videos captured from a convenience sample of unselected noncritically ill emergency department patients to create this test set of videos. We did not record the specific etiologies of the visit. For each patient, a single technician with more than 25 prior scans captured multiple video clips, for a total of approximately 2 to 4 minutes of video from different areas under the tongue using a Microscan SDF device (MicoVision Medical, Amsterdam, the Netherlands). The Microscan device was connected to an analog-to-digital converter (ADVC-110, Grass Valley, San Francisco, Calif), which digitized the video in real time and interfaced with a standard laptop computer using a FireWire (IEEE 1394a) connection. We used a custom software package to capture the digital video because the scans were conducted at the bedside (StudyMaker LLC, Charlotte, NC). Later, the files were uploaded over the Internet to a secure server where they were retrieved for offline analysis. The study protocol was approved by the local medical ethics committee of Beth Israel Deaconess Medical Center. Verbal informed consent was obtained from all studied subjects according to protocol.

The score was designed, and then we created and posted a video to http://www.MicroscanAnalysis.blogspot.com, which describes the Microcirculation Image Quality Score with example videos for each category. The first reviewer (G.N.) was involved in the score creation process and had experience analyzing the videos. We then had a second reviewer (E.L.) with experience in video analysis watch the video. Next, the 2 raters, blinded to previous scoring or clinical context, implemented the quality score metric for a set of 59 sublingual SDF videos collected from 34 unselected noncritically ill emergency department patients. A Microcirculation Image Quality Score was independently assigned to each video segment. Raters were blinded to each other's scores, and no communication regarding the videos occurred.

2.4. Data analysis

 κ scores were calculated to determine the interrater reliability for passing or failing a video, as shown in Eq. (1) [12],

$$\frac{P(a_2) - P(c_{\text{ALL}})}{1 - P(c_{\text{ALL}})},\tag{1}$$

where $P(a_2)$ is the probability of agreement between raters for unacceptable scores, and $P(c_{ALL})$ is the probability of chance agreement for each score, 0 or 1, and 10. $P(c_{ALL})$ is calculated using observed data. Eq. (1) is used to gauge pass-fail agreement by category and overall. We also calculate the correlation between rater sums as a measure of total score agreement.

3. Results

We calculated Cohen κ to assess interrate agreement using the blinded scores given by the 2 analysts for 59 videos collected from 34 patients. Total scores between raters were strongly correlated (r = 0.84). Fig. 2 shows perfect agreement ($\kappa = 1.0$) for the illumination and duration categories. Focus and pressure categories ($\kappa = 0.91$ and $\kappa = 0.82$, respectively) were highly correlated. Content and stability show substantial agreement ($\kappa = 0.76$ and $\kappa = 0.71$, respectively). Raters were instructed to fail a video for an unacceptable score in any



Fig. 2. Interrater agreement (κ), shown for unacceptable scores per category compared to overall pass-fail agreement.

category. Our results show a moderate agreement ($\kappa=$ 0.66) for an overall failing score.

4. Discussion

Side-stream dark-field sublingual videomicroscopy is used by a number of investigators to identify altered microcirculatory function through direct visualization at the bedside. This method has the potential to provide a wealth of information. However, poor image quality may prevent accurate analysis, making the videos difficult to analyze quantitatively. Technological shortcomings of current SDF imaging have been shown to require a relatively steep user learning curve with a certain degree of user expertise necessary to acquire consistent, high-quality images [9,11]. Even high-quality image sequences require time-consuming offline analysis. Some authors call for a fast and automated analysis as a requisite feature for clinical implementation [13]. Automated focus and automated light intensity adjustments during acquisition by the device are another desired feature. The advent of new technological developments shows promise in eliminating the uncertainty of pressure artifacts [11] and in providing video images with improved spatial and temporal resolution [14].

Our Microcirculation Image Quality Score provides a systematic approach for classifying sublingual SDF videos based on their image acquisition quality. The 6 categories used in this system cover many of the common areas where video quality is degraded. We have used this system to identify the highest quality clips when many or long segments of video are collected from a patient. It also provides an objective method to identify videos with deficient image acquisition quality and to categorize why the videos were deficient. We propose a schema whereby if a video falls below a certain quality, then it is not used for subsequent analysis.

Although the categories of stability, content, and pressure show considerable agreement, they have the 3 lowest κ scores in this test set, which indicates that the interrater agreement among these categories could be improved between our 2 reviewers. For each of these categories, the thresholds used for scoring are often difficult to

distinguish. Stability is ultimately dependent on the quality of the image stabilization. It is sometimes difficult to visually identify nonrigid motion of the microvascular bed, which cannot be stabilized by a simple translation model. Similarly, the content of the video is sometimes difficult to judge because it considers both the portion of artifacts blocking the field of view and the amount of looped vessels, which both rely on the rater to subjectively assess what portion of the video is affected. Partial pressure artifacts are also prone to rater bias because sluggish flow is difficult to differentiate from slight pressure.

This report has a number of limitations. First, we designed and created the image quality scoring, and our specific category system is based largely on our own experience combined with reports in the literature. We have omitted categories or incorrectly included others. The 0,1,10 scoring system is a bit untraditional, and although we found it numerically useful, better approaches may ultimately be proposed. We used videos from noncritically ill patients; it is possible that the results may be different in a population of patients with increased levels of microcirculatory flow dysfunction. With regard to our findings, our agreement was reasonable, but further training may increase the total interrater agreement, especially for the final passfail rate. Two other or more experienced reviewers may have had different agreement levels, so we are not sure exactly how well our findings may be generalized. In addition, enhancements to the scoring method may improve the scoring system. We propose only an initial approach, perhaps as a proof of concept, but believe that future improvements upon our proposed system are warranted. Finally, with the anticipated advent and improvements of analysis programs allowing for automated assessments of microcirculatory flow, image quality indicators are a necessary step between bedside image acquisition and automated data analysis. It is our hope that this and future work will provide a foundation for the development of automated image quality analysis metric that can be used to prescreen input to automated image analysis algorithms. Such a system would be the "holy grail" of clinicians to allow timely evaluation of microcirculatory function, which can be used for clinical diagnosis and managing therapy.

5. Conclusions

Our Microcirculation Image Quality Score addresses many of the common areas where video quality can be degraded. The criteria introduced are an objective way to assess the quality of image acquisition, with the goal of selecting videos of adequate quality for analysis. The interrater reliability in our preliminary study suggests that the Microcirculation Image Quality Score is reasonably repeatable between reviewers, although further assessment is warranted.

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References

- Goedhart PT, Khalilzada M, Bezemer R, Merza J, Ince C. Sidestream dark field (SDF) imaging: a novel stroboscopic LED ring-based imaging modality for clinical assessment of the microcirculation. Optics Express 2007;15:15101–14.
- [2] De Backer D, Hollenberg S, Boerma C, Goedhart P, Buchele G, Ospina-Tascon G, et al. How to evaluate the microcirculation: report of a round table conference. Crit Care 2007;11:R101.
- [3] De Backer D, Creteur J, Preiser JC, Dubois MJ, Vincent JL. Microvascular blood flow is altered in patients with sepsis. Am J Respir Crit Care Med 2002;166:98–104.
- [4] Spronk PE, Ince C, Gardien MJ, Mathura KR, Oudemans-van Straaten HM, Zandstra DF. Nitroglycerin in septic shock after intravascular volume resuscitation. Lancet 2002;260:1395–6.
- [5] Treciak S, Dellinger RP, Parrillo JE, Guglielmi M, Bajaj J, Abate NL, et al. Early microcirculatory perfusion derangements in patients with severe sepsis and septic shock: relationship to hemodynamics, oxygen transport, and survival. Ann Emerg Med 2007;49:88–98.
- [6] Tyml K, Ellis CG. Evaluation of the flying spot technique as a television method for measuring red cell velocity in microvessels. Int J Microcirc Clin Exp 1982;1(2): 145–55.
- [7] Ellis CG, Ellsworth ML, Pittman RN, Burgess WL. Application of image analysis for evaluation of red blood cell dynamics in capillaries. Microvasc Res 1992, Sep;44(2):214–25.
- [8] den Uil CA, Lagrand WK, Spronk PE, van der Ent M, Jewbali LSD, Brugts JJ, et al. Low-dose nitroglycerin improves microcirculation in hospitalized patients with acute heart failure. Eur J of Heart Failure 2009;11:386–90.
- [9] Sallisalmi M, Oksala N, Pettila V, Tenhunen J. Evaluation of sublingual microcirculatory blood flow in the critically ill. Acta Anaesthesiol Scand 2012;56:298–306.
- [10] van Beers EJ, Goedhart PT, Unger M, Biemond BJ, Ince C. Normal sublingual microcirculation during painful crisis in sickle cell disease. Microvasc Res 2008;76: 57–60.
- [11] Balestra GM, et al. Improvement of sidestream dark field imaging with an image acquisition stabilizer. BMC Medical Imaging 2010;10:15.
- [12] Cohen J: A Coefficient of Agreement for Nominal Scales Educational and Psychological Measurement. 1960, Vol. XX, No. 1.
- [13] Mik EG, Johannes T, Fries M. Clinical microvascular monitoring: a bright future without a future? Crit Care Med 2009;37(11):2980-1.
- [14] Bezemer R, Bartels SA, Bakker J, Ince C. Clinical review: Clinical imaging of the sublingual microcirculation in the critically ill-where do we stand? Critical Care 2012;16:224.