

## Review Article

# The use of laser speckle contrast imaging in clinical applications

Muhsin B. B. Khashru, Zeng T. Wang\*, Bilkis Akthar

Department of Hand and Foot Surgery, Shandong Provincial Hospital affiliated to Shandong University, Jinan, Shandong, China

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**\*Correspondence:**

Dr. Zeng T. Wang,  
E-mail: wangz\_t@126.com

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## ABSTRACT

Laser speckle contrast imaging (LSCI) is a useful device which is recruited for visualizing full-field microcirculatory images. The speckle pattern is produced as a consistent light illuminates a rough object, and the backscattered radiation is transformed into images and be shown on a screen. Movement within the object results in the fluctuation of patterns over time. Similar information can be attained by employing the Doppler effect, which needs to be scanned again. However, LSCI renders similar data without any further scanning procedure. Nowadays, LSCI has gained expanded consideration, in part because of its accelerated adoption for blood flow studies in the different surgical departments. Here we represent and review the application of LSCI methods of visualizing the field of microcirculation as medical applications from different clinical aspects and discuss the drawbacks that hinder its approval clinically.

**Keywords:** Laser speckle contrast imaging, Reconstructive surgery, Microcirculation, Flap monitoring

## INTRODUCTION

Measuring the tissue perfusion is vital in microsurgery as it helps clinicians to determine the viability of a tissue flap. Recently, there are several optical imaging techniques have been established to analyze tissue perfusion. Nowadays, most of the clinicians want a noninvasive, noncontact, easy handle, quick as well as cheap procedure.<sup>1</sup> Laser speckle contrast imaging (LSCI) is comparatively an economical, quick, noncontact visualizing method that is able to visualize a full field perfusion mapping.<sup>2</sup> LSCI works basing on the principle that a detector's spontaneous interference pattern. As a coherent laser light illuminates a rough tissue, the speckle pattern is created. Thus, when the particle moves within the tissue, provokes a variation in this speckle display causing the blurring of speckle patterns.<sup>3</sup> When the variations are triggered by the moving red blood cells (RBCs), this blurring can be accompanied by the blood flow. Starting as a slow, analog research tool, LSCI

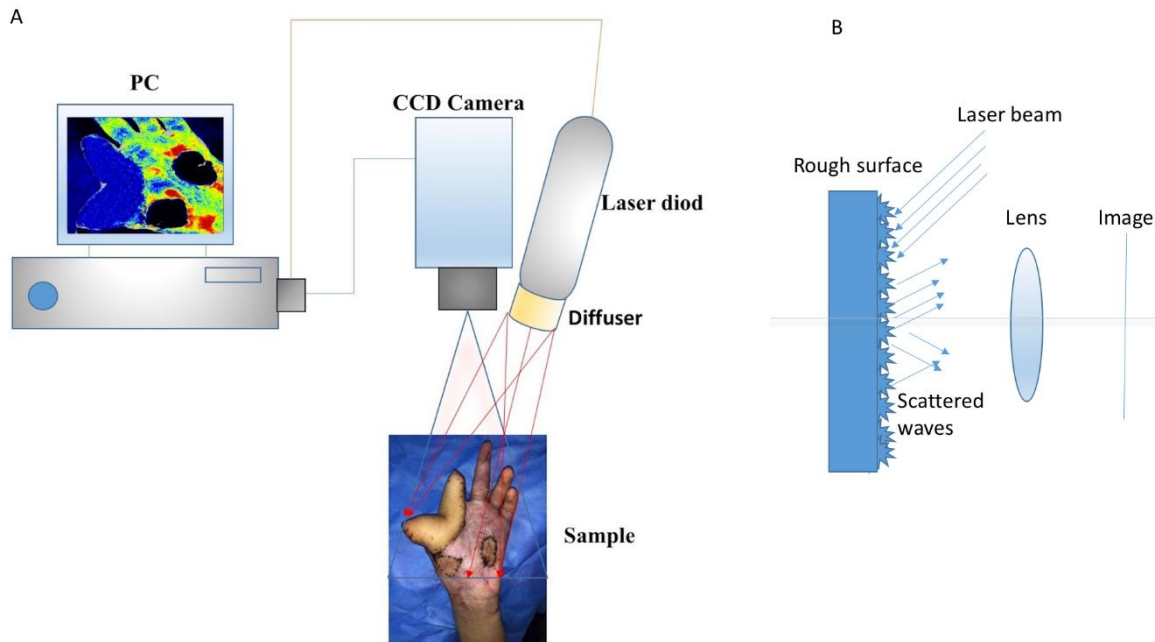
systems nowadays have gained rapid popularity to record blood flow in (near) real-time. This reason has made LSCI be approved by more clinicians into clinical practice to evaluate perfusion of different kinds of tissue, i.e., different kinds of free flaps, during replantation as well as reconstruction surgeries. LSCI has been used to image burn scalds, to check perfusion of the retina, blood flow of cerebrum (CBF), perfusion of the skin.<sup>4-9</sup> Even though many studies have been done using laser speckle, clinical applications are still very uncommon. This review presents a summary of the medical usage of LSCI currently applied by clinicians.

## THE PRINCIPLES OF LSCI

An essential task in the examination of the transferred tissue is to assess the neovascularization. LSCI is a minimal-invasive method to visualize the blood flow of superficial or uncovered vasculature. Nevertheless, visualization of deep vascular structures is comparatively difficult or impossible as the tissue hinders it. When a

scattering medium backscatters coherent light, the random interference patterns called speckle patterns to arise. Here scattering medium is usually the organic tissue. The vaguely dissimilar wavelengths of laser beam result in the gleaming of the intensity and form speckle pattern as dark and bright spots, correspondingly.<sup>10</sup> The principle of the measurement technique of the PeriCam PSI system is done by an advanced CCD camera that records these changes in the speckle pattern (Figure 1). The speckle image consists of both static and dynamic speckles. Static speckles are the result of the speckles that do not alter over time; on the other hand, dynamic

speckles change over time. These speckles are consisting of data regarding the velocity of the element or moving elements inside the object. As soon as the speckle display is produced on a motion particle, for example, red blood cells, the motion of the blood in the vessels results in variations in the speckle display on the sensor.<sup>11</sup> In the LSCI technique, the motion of blood triggers haziness of image contrast, which results in gleaming of the intensity. The result is an instant image of the microcirculation. Blood circulation amount is displayed in the arbitrary units, perfusion units (PU).



**Figure 1: (A) The basic setting of the simplicity of LSCI setting, (B) the laser speckle effect happening as a laser ray irradiates a rough diffuse area.**

This article is comprised of information taken from clinical literatures written about LSCI. The reviewed articles are selected according to the authors' interests. The formal review was done of all published literature from the last 30 years related to the application of LSCI clinically in internet-based scientific journals.

## LSCI IN CLINICAL APPLICATIONS

### *Application in reconstructive surgeries*

Flap surgery has become a popular operative procedure of reconstructive surgeries of the limbs. The success ratio of reconstructive surgeries is great; however, there are occasional failures as well. Furuta et al used the LSCI method to investigate on twenty patients having that needed excision of their tumors of the head and neck besides microvascular free tissue flap reconstruction for covering the wound and was able to find out low vascular perfusion in the edge of the tissue flap.<sup>12</sup> In some recent studies, Zötterman et al on an animal model monitored

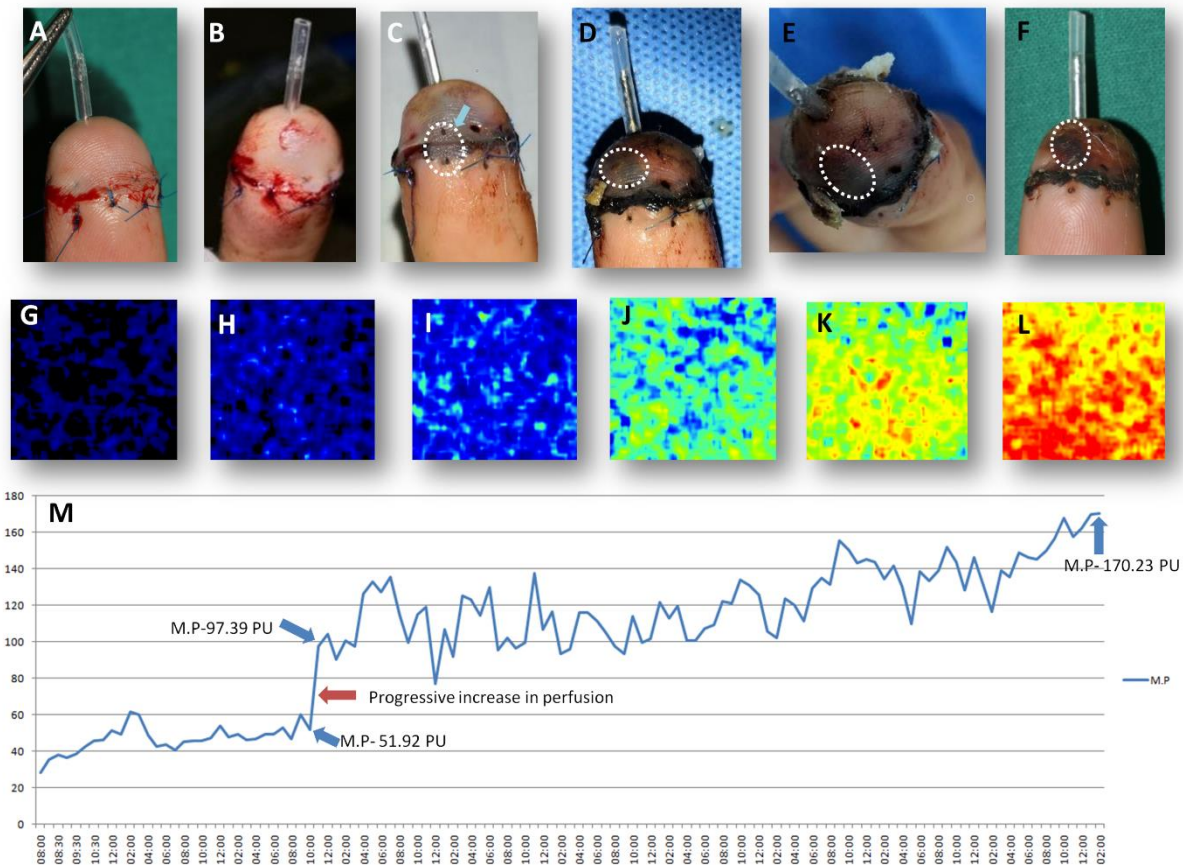
partial and full venous drainage blockade in a pig model applying LSCI technique.<sup>13</sup> They showed clear advantages in favor of LSCI, in terms of flexibility and dependability. They also used the LSCI technique to predict flap necrosis on the procaine model, which seemed to be useful for many surgeons.<sup>14</sup> In oral and maxillofacial surgery. One case study was reported on the application of LSCI for a successful finger replantation.<sup>15</sup> Recently, our group has done one pilot study on replanted fingers (Figure 2) and one case study on free flaps (Figure 3) to determine a threshold of the perfusion under which there will be the possibility of tissue morbidity.<sup>16,17</sup> In reconstructive surgeries, nowadays, the application of LSCI procedure is gaining popularity.

### *Application in plastic and burns surgery*

A burn surgeon deals on delicate tissues such as skin or the defects of muscles tissue lying superficially in most situations, unlike the rheumatologist. An example is the assessment of burn wounds. Only in about 70 percent to

80 percent of the time, the clinical assessment done by professional plastic surgeons according to their tactile knowledge is reported appropriate.<sup>18</sup> Failure to diagnose correctly may cause patients to long hospitalization period, excision, and tissue reconstruction. Therefore, there is a vital therapeutic need for a rigorous analytical process. Visualization of microcirculatory blood movement might be of excellent benefit to the plastic and

burn surgeons as it indicates the healing capacity. LSCI; otherwise, it can achieve parallel outcomes while maintaining the advantage of being minimal-invasive and non-contact with the additional benefit of being inexpensive, simple and with swift data collection.<sup>19</sup> LSCI is essential for the treatment of patients who cannot remain still or because it concerns infants.



**Figure 2: (A-F) Typical visual images of an 18-year-old female replanted rt. middle fingertip (Guillotine type, door crush injury, Tamai zone I amputation). Despite the usual appearances of (A and B) on postoperative and 1st POD respectively, however, their corresponding contrast images (G and H) show low perfusion ROI. Cautious observation without any intervention was taken. Hereafter, few stitches were removed on 2nd POD (C); white dotted area), the tension was decreased, showing noticeable improvement in perfusion (I), rising to 97.39PU from as low as 51.92 PU (M) forming a saw-tooth like graph of the perfusion curve. However, the dark tint of the skin (D-F), white dotted circles) lingered, yet, the corresponding contrast images (J-L) show tremendous improvement in perfusion, and is evident in (M) with maximum perfusion of 170.23 PU on 7th POD [ $p < 0.0005$ ].<sup>16</sup>**

The initial report of the LSCI application to evaluate microcirculation in burn surgery was by Stewart et al.<sup>19</sup> The group evaluated the perfusion of burn scar and compared LDI to LSCI, finishing with a positive note to LSCI. In a mouse burn model, Crouzet et al used LSCI to record perfusion.<sup>20</sup> The findings show that LSCI can differentiate the statistical significance concerning superficial and deep burns. Such findings are auspicious even though, because of the massive biological differences in the skin, for example, thickness and structure conversion to clinically relevant evidence could

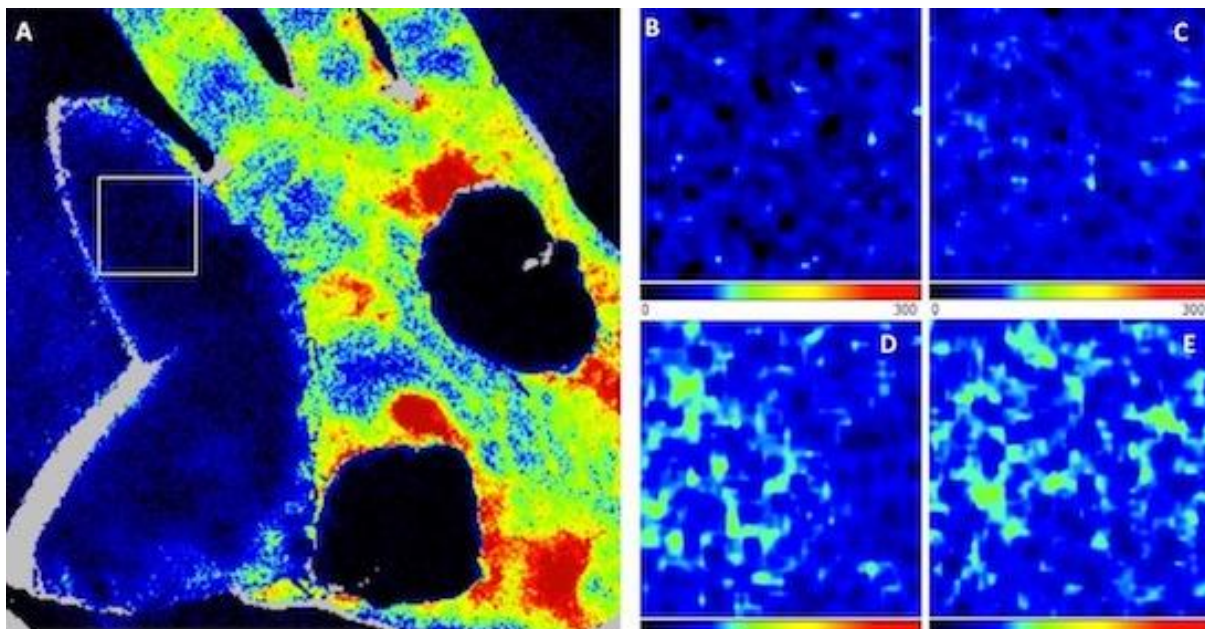
be difficult. A study was conducted by Lindahl et al on scald injuries of babies that attempted to portend the burn consequences two weeks after burning.<sup>21</sup> As LSCI collects data swiftly, it is well adapted for pediatric burn. The group reported a significant difference from those who received treatment after one day for wounds that recovered within two weeks. LSCI allows with simply understandable images to portend wound healing. By evaluating one microcirculatory calculation is adequate deciding next step. Together with the experience of the surgeon, LSCI should be a useful tool

to measure the micro circulation for the surgeon to make critical decisions for burn injuries.

### **Application in neuroscience**

As per the study of Dunn et al, the technique has been developed over the past decade as it has been used by the neuroscience community to calculate blood flow in the brain.<sup>22</sup> There have been over 100 publications on the subject over the past eight years, meaningfully developing the concept and application of LSCI.<sup>23</sup> In a neurosurgery, the determination of CBF level pre-operatively is fundamental in confirming the post-operative tissue morbidity.<sup>24</sup> It was initially experimented on rodents.<sup>25</sup> Subjects of studies were gone through not only some artificial stimulations, such as electrical stimulation but also gone through some physiological stimulations such as hyperthermia.<sup>26</sup> previous studies has shown the success of LSCI technique on clinical

applications. Hecht et al. described the earliest clinical study done on three patients using LSCI to monitor CBF intra-operatively.<sup>27</sup> They reported LSCI to be a promising method as an expansion of microcirculation was perceived just after anastomosing the vessel. Hecht et al, in their another study performed direct surgical revascularization on thirty patients and found some similar favorable outcomes regarding the application of LSCI clinically.<sup>28</sup> Nomura et al, in their research compared LSCI to PECT and described a reasonable success.<sup>29</sup> Other related uses of LSCI are the estimation of infarction the malignant stroke and functional brain mapping. Upcoming studies should include an accumulation of a large number of information about the evaluation of CBF to resolve different limits, that may help the clinicians to decide the further management. As a result, LSCI may be taken as a standard of neurosurgical approaches within neurosurgery.



**Figure 3: LSCI image of the hand showing the typical perfusion in both tissue flap and the palm on post-operative day 1. The white rectangle on (A) represents the chosen ROI, as it was the distal portion of the flap which was considered under danger, (B) development in perfusion on the third day followed by (C) on fifth day, (D) on sixth day and (E) on seventh day. The two dark round things are made of sterile gauze to create pressure on skin grafted area.<sup>17</sup>**

### **Application in ophthalmology**

The application of LSCI in ophthalmology has gained a lot of popularity recently. Generally, two kinds of laser diodes are used in ophthalmic researches; one is used for measuring deep perfusion; another one is a blue module argon laser for measuring superficial perfusion depending on the application is used. The flow of choroid supplies, their tissues and the external retinal layer, and their circulation supplies the inner retina. The earliest digital

application of LSCI was made by Tamaki et al, to measure the blood circulation of retina, blood circulation dynamics of the choroid, and optical nerve head.<sup>30</sup> It was then developed to test the choroid and ONH of the human eye in real time.<sup>31</sup> Up till now, LSCI has been used in monitoring perfusion in retina. Yaoeda et al, Ruth in 1994 monitored optic nerve perfusion.<sup>32</sup> Tomidokoro et al in 1998 monitored iris using LSCI technique.<sup>33</sup> Separable features such as sex, glaucoma, and hemodynamic values are said to be associated with the factors that pulse

waveform provides.<sup>34</sup> Although, numerous reports in ophthalmology were done previously, there is still a need of further research on the application of LSCI to improve the understanding of the parameters that varies in different diseases.

### **Application in dermatology**

Port-wine stain marks are examined using the LSCI technique recently in dermatology. PWS is progressive and associated with abnormalities of blood vessels causing increased blood flow locally. The outcome of Pulsed dye laser treatment on the microcirculation of blood was first examined by Huang et al.<sup>35</sup> They reported a notable lower perfusion in the areas having treatment although a natural perfusion was observed in the healthy area. This suggests that LSCI is a promising guidance tool for surgeons to minimize the number of periods required for the full whitening of PWS.<sup>36</sup> LSCI may be used to analyze ulcers of diabetic foot that could go through local necrosis recorded by Mennes et al.<sup>37</sup> LSCI has made it possible to be clinically recruited in dermatology.

### **Other application of LSCI**

There are some other interesting uses of LSCI are applicable in reconstructive surgeries, rheumatology and dentistry. In oral and maxillofacial science LSCI has been applied to image the gingival blood flow, dental pulp flow.<sup>38</sup> In cardio vascular studies there are numerous uses of LSCI. Even in general surgery LSCI technique had been used, Cheng et al in 2003 monitored mesentery.<sup>39</sup>

### **Limitations of laser speckle device**

As explained previously in a plenitude of forms, a few abridgements that hinder the application of this technique in clinical conditions. Number one, maximum investigations are restricted in measuring the superficial perfusion value. Secondly, this appears to be a difficulty for recording the tissues with the motion, for example, intraabdominal perfusion analyses as well as patients such as Parkinson's disease patients who cannot remain still. However, latest studies propose a reference zero flow patch to be favorably applied to diminish the movement artefacts in LSCI data processing.<sup>40</sup>

## **CONCLUSION**

It is obvious that there is a considerable number of activities around the globe involving LSCI procedure. Notwithstanding, LSCI has been applied in different sectors for above 25 years; the basic method has remained comparatively unchanged. LSCI has several strong points, such as simplicity and inexpensiveness; however, the main weakness is the relatively low real-time spatial resolution. However, a significant amount of analysis is yet required to increase better understanding of the device.

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