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An Overview of Quantitative Capillary Refill Time: Measurement and Application in Clinical Practice

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Abstract

Capillary refill time (CRT) is a vital clinical parameter used for the evaluation of peripheral perfusion status in emergency departments and critical care settings. Commonly used manual measurements lack a true criterion standard and are based on visual inspection of fingertip color, leading to low inter-observer reliability. Recent advances in spectroscopic and imaging technologies have made CRT measurement quantitatively significant (Q-CRT), thus enhancing its reliability and accuracy. Light intensity transmitted through the fingertip correlates with blood volume and can be measured using a pulse oximetry sensor. The time required for the transmitted light intensity to return to 90% of the original value after pressure application is defined as Q-CRT. In addition, certain technologies can evaluate Q-CRT via analysis of reflected light in various areas of the peripheral surface. Like manual CRT, Q-CRT is influenced by several factors, including temperature, anatomical measurement sites, gender, and age. However, for Q-CRT, the influence of other confounding factors (light conditions, intensity of applied pressure, "naked eye" assessment) on the measurement outcome is reduced or eliminated. Q-CRT correlates with standardized manual CRT, but it systematically shows higher values. The initial investigations have indicated that Q-CRT could be used to predict sepsis and to assess postoperative outcomes following liver transplantation.

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1. Introduction

Capillary refill time (CRT) is a rapid prognostic indicator that is used to evaluate tissue perfusion status.[1] CRT measurements are performed in emergency departments, critical care units, and emergency situations outside the hospital. In addition, the current COVID-19 outbreak has shown the significance of CRT as an early prognostic indicator in patients.[2,3] CRT is a simple, fast, and non-invasive measurement that can be lifesaving in critical situations. When blood volume is substantially decreased in the human body, blood is centralized to ensure the perfusion of the most important organs. The resulting decrease in peripheral perfusion is reflected by prolonged CRT. The measurement of CRT, therefore, enables the assessment of shock status and can determine the need for preventive and therapeutic interventions. The prolongation of CRT also correlates with the degree of hypovolemia (dehydration) in children.[1]

The CRT concept was first introduced by Beecher *et al*.[4] in 1947, who interpreted it as "normal", "definite slowing" or "very sluggish", corresponding with the normal condition, slight/moderate, and severe shock. Champion *et al*. defined a "normal" CRT to be less than two seconds in 1980 on an arbitrary basis.[5] For the manual measurement of CRT, the fingertip of the patient is compressed until blanching occurs. The time until the fingertip has regained its original color after compression is defined as CRT. A CRT of 2 seconds is usually considered the upper limit of normal.[6] The main disadvantage of manual CRT measurement is its poor inter-observer reliability,[7] which may result from differences in applied pressure or difficulty in defining the time point at which the

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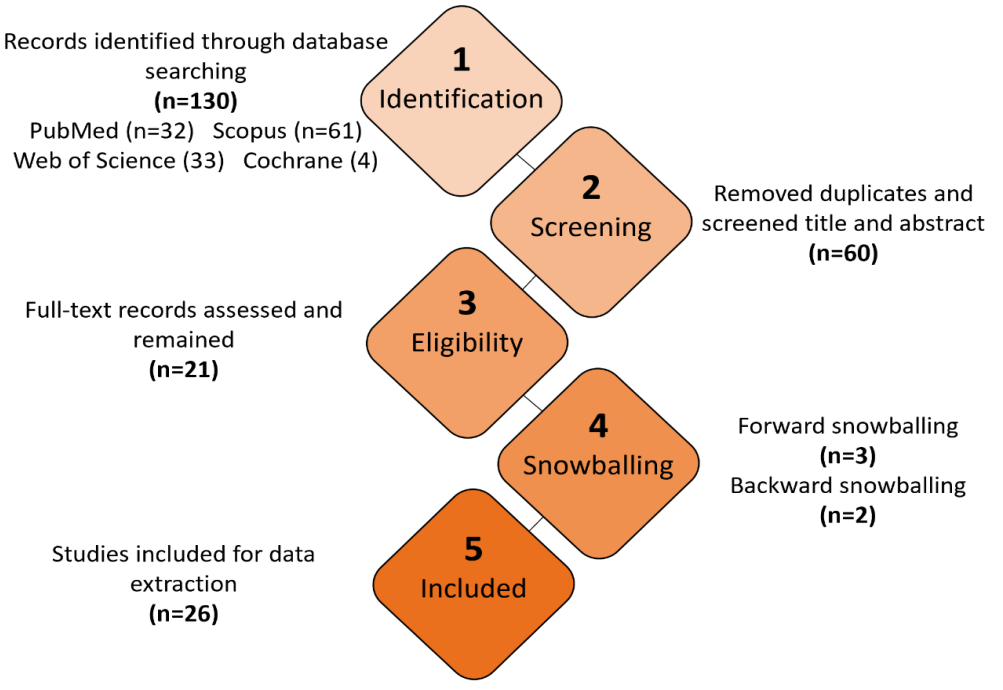

Fig. 1: Data identification, screening, eligibility, snowballing and inclusion.

fingertip has regained its original color. The dependency on "naked eye" inspection and the lack of standardization of the actual blanching maneuver may therefore be contentious issues. Furthermore, CRT is affected by several additional factors like size, form, and temperature of the measured spot, as well as the gender and age of the patient.[1]

Recently, an increasing number of studies have focused on the development and application of novel technologies for the quantitative measurement of CRT (Q-CRT), in which the spectroscopic technology of a pulse oximeter with a blood oxygen saturation (SpO2) sensor combined with video mode polarization spectroscopy is used. In this work, the functioning principle, advantages, and limitations of this measurement method are described. Additionally, the question is addressed whether the enhanced measurement mode improves the accuracy of CRT measurements compared to the traditional manual method. Finally, the applications and prospects of Q-CRT measurement in the emergency department and intensive care unit are described.

A broad literature search was performed in the following databases: PubMed, Scopus, Web of Science, and Cochrane Library using the following syntax options: (("capillary refill time" OR CRT OR "capillary refill") AND ("quantitative CRT" OR "pulse oximeter" OR "pulse oximetry")) OR ("capillary refill index" OR "blood refill time"). The selection process is described in Fig. 1. All papers published up to 15.06.2024 were included.

One hundred thirty records were identified by our set of queries, after excluding the duplicates, 60 remained. Of these, 39 articles were excluded at the full-text assessment level. Five papers were selected by backward snowballing (examining the lists of references of the selected papers) and forward snowballing (considering the citations) using Google Scholar. Twenty-six articles were found to meet the inclusion criteria to describe the measurement of Q-CRT and were used in the analysis.

2. Techniques for measuring peripheral perfusion

Examination of peripheral blood perfusion status is a key strategy for supporting high-quality patient care and population health management. Methods of perfusion measurement, emerging in the 1970s and 1980s, included pulse oximeter-aided photoplethysmography, laser doppler flowmetry (LDF), and laser doppler perfusion imaging (LDPI).[8,9] Recent innovations in technology have opened up increasing opportunities to observe and measure peripheral perfusion in various aspects, including laser-based methods (multi-exposure laser speckle contrast imaging - MELSCI) and polarization spectroscopy imaging - PSI (alias tissue viability imaging - TiVi) to capture and quantify the capillary refill process.[10,11] The most popular techniques nowadays include:

A) visual and tactile clinical assessment (warmth or coldness of the skin, CRT, mottling score);

B) thermographic body temperature gradient mapping (*e.g.*, central-to-peripheral, peripheral-to-ambient, or forearm-to-fingertip skin temperature gradient);

C) near-infrared spectroscopy, sublingual capnometry and pulse oximetry (different values can be measured, including partial pressure of carbon dioxide, peripheral perfusion index, peripheral oxygen saturation SpO2, as well as myoglobin and cytochrome aa3 oxidation);

D) orthogonal polarization spectroscopy (functional capillary density);

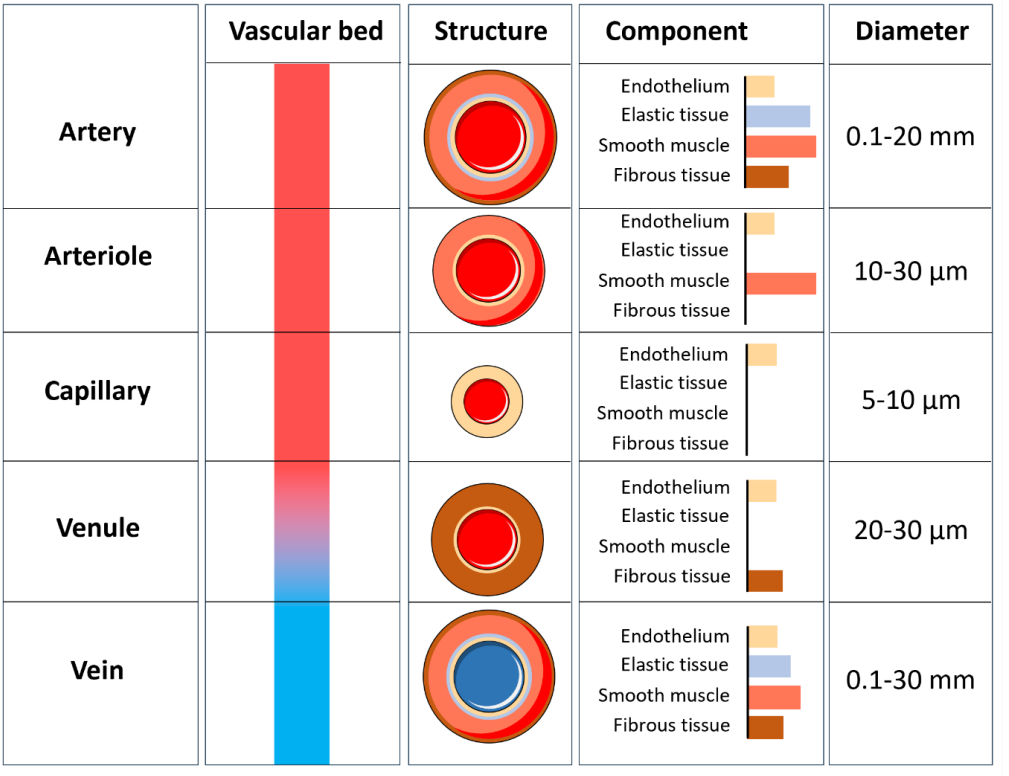

Fig. 2: An overview of the various cutaneous vessels, including their features.

E) laser dropper flowmetry (microvascular blood flow).[12]
A number of recent studies have pointed to the morphological (vessel density, perfused vessel proportion, vessel diameter), dynamic (vascular blood velocity, RBC concentration), and functional (pharmacological tests based on vasoactive drugs, post-occlusive reactive hyperemia tests) parameters of non-invasive measures.[13-15] Furthermore, microvascular perfusion can be evaluated by either "single-point" or imaging methods, which provide a full-field view of the microcirculation pattern.[16] Measurements can be performed either intermittently or continuously, depending on the desired temporal resolution.[17,18] In addition, methods that combine direct visualization and quantitative evaluation are becoming increasingly available to clinically assess peripheral circulation.

From an anatomical perspective, the skin and systemic microcirculation encompass the vascular region from arterioles to venules, including the capillary network composed of vessels measuring less than 20 microns (Fig. 2). Arterioles and venules possess vascular smooth muscle cells that can react to various mediators and modulate capillary blood flow.[19] Capillaries serve as the primary site for the delivery of essential nutritional and non-nutritional components to tissues, defined as vessels measuring less than 10 µm in diameter and accommodating a single file of red blood cells.

The differentiation between perfusion (the volume of blood supplied to the capillary beds of a tissue segment over a specified time, measured in mL of blood per 100 g of tissue per minute) and flow (the volume of blood traversing a vessel per unit of time) is crucial for comprehending the function of arteriovenous anastomoses. The narrowing of arteriovenous anastomoses reduces blood flow to capacitance channels like venules and impacts the perfusion pressure of capillaries. August Krogh demonstrated through sophisticated experiments in the 20th century that the intercapillary distance in tissues significantly influences oxygen delivery, with reduced pO_2 tension correlating to diminished oxygen transport along the capillary.[20] As tissue oxygen demand escalates, a greater number of capillaries must be perfused.
Falotico *et al.*[21] categorized the methods according to their main mechanism of monitoring perfusion status, which can be (a) capillary refill, (b) reflected light (surface color changes), (c) transmitted light (spectrophotometric), and (d) temperature measurement. These techniques can be further delineated as either subjective or objective methods. In technologies measuring reflected light, big progress has been made in eliminating the variability inherent to manual inspection, in order to objectively quantify CRT.[22] For instance, as an important criterion, the peripheral perfusion index (PPI) has been proposed. PPI is derived as the ratio of pulsatile blood flow to non-pulsatile blood flow in the monitored tissue.[23] It is now broadly used in hemodynamic monitoring and can be assessed in several non-invasive or minimally invasive ways, of which CRT is one of the most well-known.[24]

2.1 CRT and Q-CRT measurement principles

Capillary Refill Time can be easily measured quantitatively using the signal output of a pulse oximeter equipped with a SpO2 sensor. Prior to explaining the measurement principle of

Q-CRT, the basic working principle of pulse oximetry will be described.

2.2 Working principle of pulse oximetry

A pulse oximeter with a SpO2 sensor is designed to measure the peripheral oxygen saturation of arterial blood non-invasively. As a rule, it emits light of two different wavelengths (660 nm and 940 nm) and measures the intensity of light transmitted through the tissue (mostly the fingertip) with a photodiode located on the opposite side. The difference in light absorption of oxygenated hemoglobin (HbO2) vs. deoxygenated hemoglobin (Hb) enables the calculation of oxygen saturation. Although HbO2 absorbs higher amounts of infrared light (940 nm wavelength) and less red light (660 nm), it is vice versa for Hb.[25] Besides the transmissive approach, there are also pulse oximetry systems that measure the light reflected from the tissue. In these, the photodiode is located on the same side as the light-emitting diode.[26]

Blood volume changes periodically in the arteries due to the cardiac cycle, while remaining nearly constant in the veins and capillaries. Hence, periodic changes in blood volume in the arteries lead to a pulsatile signal component that can be distinguished from the constant blood signal in the veins and capillaries and from the signals of other tissues (fat, bones, skin). The waveform of the light intensity at different wavelengths that is transmitted through (or reflected from) the tissue over time is recorded.[25]

Waveform analysis-based full-finger reperfusion time (FFRT), which was previously referred to as "Blood Refill Time," has been suggested as an alternative to conventional clinician-measured CRT.[27] This device utilizes pulse oximetry to measure CRT by analyzing light transmission through the fingertip. It determines the CRT by measuring the time it takes for the blood to return to the digit following a standardized blanching operation and the subsequent relaxation of compression. A moderate correlation has been observed between clinician CRT and FFRT.[27,28]

2.3 Principle of Q-CRT measurement

The strong absorption of light at 660 nm and 940 nm by hemoglobin can be utilized to quantitatively measure CRT using the signal output of a pulse oximeter equipped with a SpO2 sensor.[29] Fig. 3 shows the measurement principle of Q-CRT, assessing the transmitted light intensity. Compressing the fingertip results in the expulsion of blood from the finger. According to Beer-Lambert's law, this leads to a decrease in light absorption. Hence, there is an increase in light transmission, which is measured by the pulse oximetry sensor. When pressure is released, the vessels are refilled with blood, and the amount of transmitted light decreases. In some studies, only measurement data from infrared light (940 nm) is used to obtain Q-CRT values.[29-32]

Pressure is applied either manually or with a fingertip compression device consisting of an air pump and an inflation bladder.[29-33] In some cases, no pressure application method is specified.[34-36] The applied "firm pressure" typically ranges between 400 mmHg and 500 mmHg.[29-31,34-36] In one study, the pressure was specified as "high enough that no pulsatile component of reflected light can be observed".[33] Pressure is applied for approximately 5 seconds in all cases. In all the

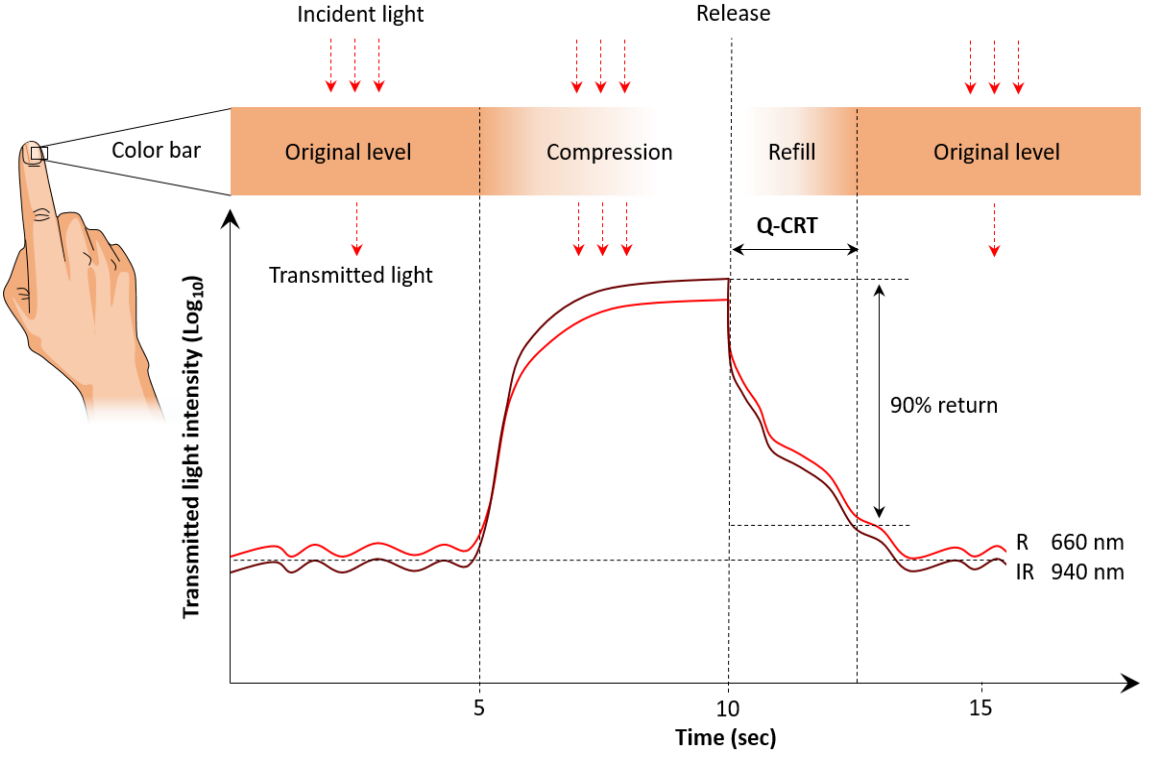

Fig. 3: Measurement principle of Q-CRT using a pulse oximeter. Because blood is a major absorber of red and infrared light, the transmitted light intensity increases when blood is squeezed out of the fingertip.

included studies, Q-CRT is defined as the time in seconds taken from pressure release until the transmitted (or reflected) light intensity (or fitted curve) reaches 90% of its original level.[29-31,35] Waveform data collected during the measurement is stored and Q-CRT is assessed on a personal computer afterward in some studies.[30,32] However, Q-CRT can also be displayed directly on the measurement device in another setup.[36]

There are also reflected light-based approaches for Q-CRT measurements. Liu *et al*.[33] examined the reflected light intensity at an emission wavelength of 850 nm, whereas Wang *et al*.[37] used a peak emission wavelength of 420 nm. For different wavelengths, tissue penetration depths differed significantly. The light intensity at 420 nm provides information mainly about blood flow in the upper skin capillaries, corresponding to penetration depths less than 150-200 µm.[38] A light wavelength of 850 nm penetrates deeper into the tissue (around 1250 µm), yielding information about a broader tissue region.[38] Since there is a variation in the depth of penetration and absorption over the range of wavelengths,[39,40] the intensity of light scattering/diffusing through the skin and emerging from the tissue can be represented as the "banana-shaped" fashion (Fig. 4).

In contrast to fingertip assessment, certain studies evaluate Q-CRT via different analyses of reflected light from various peripheral surface areas. John *et al*. used TiVi, a digital photographic technique based on polarisation spectroscopy, to quantify RBCs after the release of blanching pressure during the CR test. The sites examined included, together with left index finger pulp and dorsum of the left index finger, left volar forearm, sternum, and forehead.[22] Crook *et al*.[41] assessed the concordance between fingertip and sternum CRT in children. The findings indicated that fingertip CRT varied between 0.05 and 2.78 seconds, with a mean of 1.08 ± 0.44 seconds. The sternum CRT, on the other hand, ranged from 0.85 to 2.38 seconds, with a mean of 1.5 ± 0.33 sec. The fingertip and sternum CRT measurements showed a significant difference ($t = -9.2$, $df = 91$, $p=<0.001$), indicating a weak correlation between the two CRT measurements ($r = 0.18$, $p = 0.9$).

Kerr *et al*.[42] introduced a novel approach that calculates CRT by applying a safe, pre-calculated force to the subject's forehead with the Shadow Robot Hand and a BioTAC sensor for a duration of 5 seconds. The results suggested that the proposed method enabled a more precise CRT measurement than that of a medical professional. The predictive value of CRT during septic shock was analysed by Ait-Oufella *et al*.,[43]

Table 1: Comparison of factors affecting manual CRT vs. Q-CRT measurement outcomes.

Influencing factor	Manual CRT	Q-CRT
Temperature	increased at lower T	increased at lower T
Age	higher CRT in the older population	tendency of higher Q-CRT in the older population *
Light conditions	dependent	independent +
Applied pressure	manually, no quantification	compression device with inflating bladder (not in all studies) intensity: 400 mmHg or 500 mmHg duration: 5 seconds
End of measurement	visual inspection	cut-off value: 90 % of transmitted light intensity before compression

Note: * small sample size, + no experimental investigation.

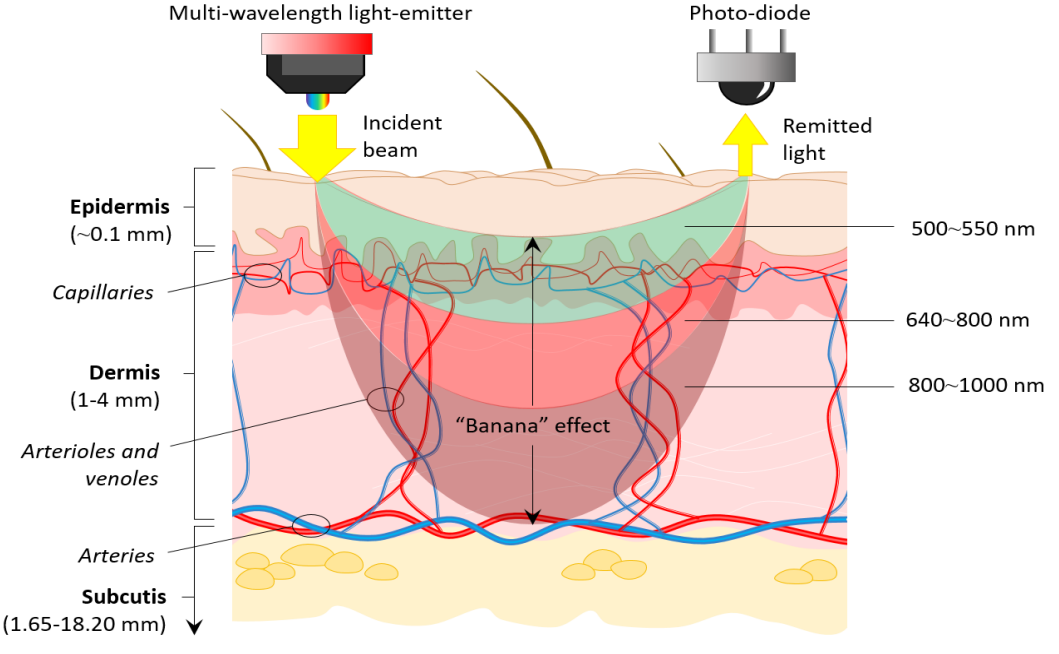

Fig. 4: "Banana" pattern of reflectance through the skin for light of different wavelengths.

who also compared measurements at two sites: the classical index fingertip and knee area. The CRT measured at both locations was significantly higher in non-survivors than in survivors (5.6 ± 3.5 vs 2.3 ± 1.8 seconds, $p < 0.0001$ for index CRT and 7.6 ± 4.6 vs 2.9 ± 1.7 seconds, $p < 0.0001$ for knee CRT). La Via *et al.*[44] posited that CRT measurements obtained from the finger using a standard method may be equivalent to those recorded at the earlobe; however, CRT values measured at the finger in various anatomical positions would differ.

2.4 Factors influencing CRT/Q-CRT

Several factors can influence the CRT value. Some of these effects are caused by the observer-dependent principle of manual measurement and can be eliminated by Q-CRT assessment using a pulse oximeter. Other conditions are related to physiological changes in peripheral perfusion and thus affect Q-CRT (Fig. 5). Those conditions must be considered when interpreting the results (Table 1).

A decrease in skin temperature is associated with prolonged manual CRT values in adults as well as in children.[1] This correlation was also observed in Q-CRT measurements. For instance, in a study involving healthy adult volunteers, when the fingertip temperature was decreased by immersing the hand in a water bath at 15 °C before measuring Q-CRT in a temperature control box at 15 °C, the Q-CRT values were found to be significantly higher than those measured at room temperature ($p<0.01$).[29] Furthermore, Q-CRT exhibits sensitivity in identifying temperature-dependent peripheral perfusion anomalies across age groups, accurately reflecting the physiological alterations linked to hypothermia. Comparable trends were found in studies on pediatric and geriatric populations, suggesting that measurement reliability is constant under severe temperatures.

CRT and Q-CRT are prolonged in older patients.[1] On average, CRT increases by 3.3% per decade of life.[45] This trend is also observed in Q-CRT, in which older adults systematically exhibit higher values than younger cohorts. Research comparing Q-CRT to manual CRT demonstrated that Q-CRT was reliable in older patients, with a much lower inter-observer variability (mean coefficient of variation: 15% vs. 28%, $p < 0.05$).[29] Given this, Q-CRT serves as a reliable tool for evaluating peripheral perfusion in geriatric settings, where subjective interpretations may render manual methods difficult. However, controlled tests employing a range of skin tones under different light conditions have shown that the self-emitting light source of Q-CRT devices maintains independence from ambient lighting.[46] These results bolster Q-CRT's dependability in settings where manual CRT proves unreliable.

Additionally, Q-CRT has proven to be highly reliable for all skin tones. Q-CRT demonstrated a consistent measurement range with a coefficient of variation < 10% for all skin types in a clinical experiment with 150 individuals representing Fitzpatrick skin types I-VI.[46] This stands in stark opposition to manual CRT, which showed a divergence of almost 30% in those with darker skin because it was difficult to see color return and blanching. These findings highlight the potential of Q-CRT to eliminate racial biases in manual CRT and transform it into a more equitable clinical tool.

The measurement results of manual CRT significantly differ between light and dark conditions.[47] Therefore, sufficient illumination is required to accurately assess this parameter by visual inspection. Regarding Q-CRT, to date, no experimental investigation has been conducted concerning this aspect. It may be assumed that light conditions do not influence Q-CRT, because the required light is emitted by the device itself, and the cut-off value to stop the Q-CRT time counting is a relative value (90% of the transmitted light intensity before compression).

In many cases, the duration and intensity of applied pressure are not precisely quantified in manual CRT measurements. Differences in these parameters can affect the measurement outcome.[1] In most Q-CRT measurement

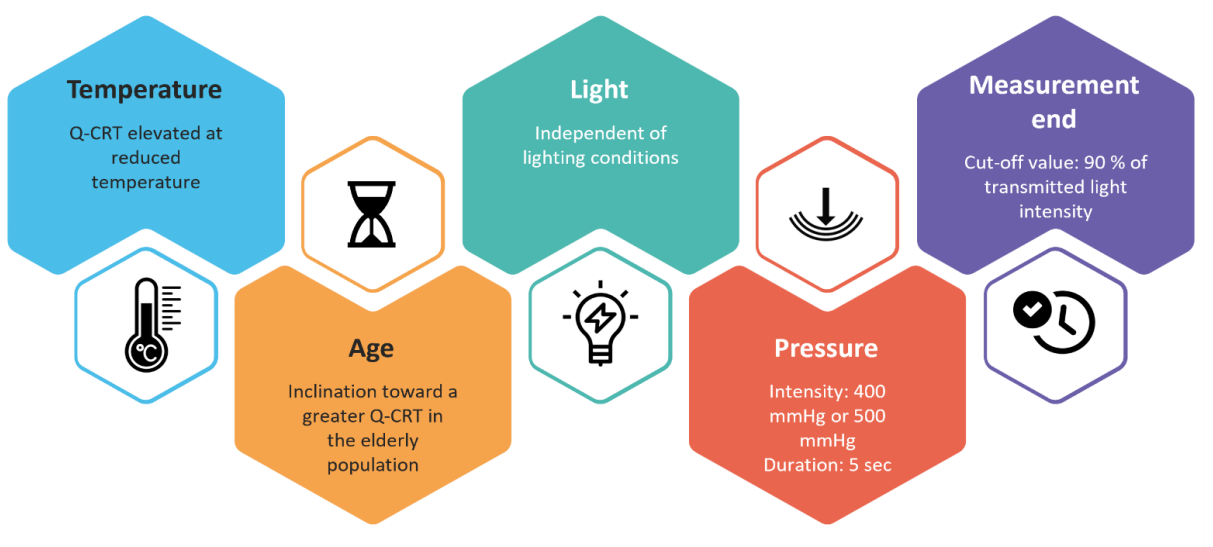

Fig. 5: Variables influencing the results of Q-CRT measurements.

settings, a pressure device consisting of an inflation bladder is used to control the duration and intensity of the applied pressure.[29,31,32,36] In manual CRT measurements, the time point, at which the fingertip regained its original color as the end of time measurement is not easy to determine exactly. This is likely to cause inaccuracies and lower reliability. The measurement principle of Q-CRT enables a standardized cut-off value for this purpose. The technique's consistency across various operators and patient groups has been confirmed by studies employing automated pressure devices for Q-CRT, which have presented an intra-rater reliability of 0.92 (95% CI: 0.87-0.96) and an inter-rater reliability of 0.89 (95% CI: 0.83-0.94).[32]

Nagasawa *et al*.[48] conducted a recent study that analyzed CRT on the interior side of the forearm, investigating the impact of finger pressure on CRT measurements. They employed an RGB camera to monitor the color shift in the compressed area following the pressure release. In comparison to compression applied by weight (1.6 seconds), compression applied by finger resulted in prolonged CRT (2.1 seconds). The difference may be attributed to the fact that the former was higher (3.0 N/cm^2) than the latter (1.6 N/cm^2), and no real-time feedback on the compression by the finger was provided during the experiments.

In CRT, gender inequalities were also noted, and Q-CRT likely represented no exception. Male patients typically have lower CRT values than female patients, which may be because of hormonal variations that affect peripheral vascular tone.[49,50] In a recent study, the mean difference between male and female Q-CRT was 0.2 s ($p = 0.03$); however, there was no discernible change in the method's diagnostic accuracy between the two genders. These findings imply that, despite slight differences, Q-CRT remains a valid assessment for individuals of both genders, and further studies could improve gender-specific standards.

Furthermore, John *et al*.[22] demonstrated a large variability in Q-CRT (shown as Q-CR curves) between different anatomical sites, and their temperature was shown to be a key factor influencing Q-CRT. The same authors conducted another study that found that the forehead had markedly less variability in temperature and Q-CRT, supposedly due to less arteriovenous anastomoses (AVAs) when video mode polarization spectroscopy was used. Skin areas containing more AVAs are more prone to react to sympathetic adrenergic stimulation.[51]

Dehydration induces peripheral vasoconstriction and a decrease in intravascular volume, which significantly increases the CRT. In this physiological reaction, blood flow to vital organs takes precedence over peripheral circulation. Fage *et al*.[52] reported that volume expansion with a 500 mL saline infusion dramatically decreased CRT in patients with septic shock, emphasizing the importance of hydration status in peripheral perfusion measurements. These findings are especially relevant in acute care settings because CRT is commonly used as a rapid diagnostic tool. CRT readings that are misleadingly prolonged because of dehydration may require unnecessary interventions. This result highlights the importance of fluid status evaluation in CRT and Q-CRT interpretation. Future research should investigate the accuracy of Q-CRT for detecting minute perfusion changes caused by dehydration in patients with different demographics.

For individuals with darker skin, the repeatability and reproducibility of CRT measurements are restricted. Q-CRT measurements presented by Bachour *et al*.,[46] demonstrated excellent performance and repeatability across all Fitzpatrick skin phototypes. The findings suggest that 80% of the CRT measurements fell within ±20% of the expected CRT value. Single-point Q-CRT measurements are likely less conclusive than repeated measurements (e.g. imaging and monitoring methods). However, very few studies have investigated the effect of single or repeated measurements on Q-CRT.[53] Blood lactate levels and other clinical parameters have demonstrated a strong association ($r = 0.88$, $p < 0.001$) with repeated measures in critically sick patients, such as those in intensive care units, suggesting that these parameters may be used to track trends in perfusion status instead of isolated examinations.[30]

3. Evaluation of measurement performance

Due to the lack of a gold standard for CRT measurements, the choice of reference to evaluate the performance of Q-CRT is not trivial. Shinozaki *et al*.[32] compared Q-CRT measurements with standardized manual measurements of CRT using a chronometer and standardized pressure application duration. As another reference method for Q-CRT, videos of the capillary refill process were analysed algorithmically using image-analysis software.[31] The measurements of both studies were performed in the emergency department (ED). For video-based comparison with Q-CRT, additionally 30 healthy volunteers were also included.

There was a strong correlation between manual standardized CRT and Q-CRT ($r = 0.723$, $p < 0.001$),[32] as well as between video-based CRT and Q-CRT ($r = 0.89$, $p < 0.001$ for healthy people; $r = 0.76$, $p < 0.001$ for patients in the ED.[31] Nevertheless, a systematic bias was found between Q-CRT and the reference methods: Q-CRT was associated with longer refill times than video-based CRT (healthy people: +1.1 seconds, patients in ED: +1.7 seconds) and manual CRT (+1.95 seconds). The ability to predict hospital admission from the ED did not differ between manual CRT and Q-CRT. The best cut-off value for Q-CRT to predict patients' admission to the hospital was found to be 2.74 seconds, yielding 83% sensitivity, 61% specificity, 59% positive predictive value, and 85% negative predictive value.[32]

Inter-rater reliability of the tests has not been evaluated, as typically only one examiner performed all measurements. Intra-rater reliability for average measures showed slightly better values for manual CRT (0.92, 95% CI: 0.85-0.96) than for Q-CRT (0.88, 95% CI: 0.79-0.94). The same was true for single measures (manual CRT 0.79, 95% CI: 0.66-0.88 vs. Q-

CRT 0.72, 95% CI: 0.55-0.84).[32]

CRT can also be quantified by means of polarization spectroscopy at a correct and conclusive level.[22] John *et al*.[53] compared naked-eye assessment with Q-CRT using polarization spectroscopy imaging to measure intra- and inter-observer agreement in CRT estimations among medical and nonmedical volunteers and to evaluate the agreement between "man" and "machine". Intra-observer repeatability was low, as was inter-observer agreement. The authors concluded that the ability of "man" to assess the time to return to normal color was poor compared with Q-CRT measurements.[53]

4. Applications of Q-CRT

Q-CRT measured in patients at admission to intensive care units (ICUs) directly after liver transplantation is significantly correlated with the postoperative length of ICU and hospital stay.[35] Additionally, there is a significant association between Q-CRT upon admission to the ICU with the total amount of ascitic discharge for 14 days after surgery. These correlations do not exist for Q-CRT measured one day after surgery nor for the change in Q-CRT from admission to one-day post-operation.[35] Another potential application of Q-CRT is sepsis prediction and control. Q-CRT values are significantly higher in patients with sepsis than in other patients in the emergency department ($p < 0.001$).[36] As a predictor of sepsis, Q-CRT is comparable with the quick sequential organ failure assessment (qSOFA) score (area under the curve (AUC) 0.74 and 0.83 respectively), systemic inflammatory response syndrome (SIRS) score (AUC 0.61) and lactate level (AUC 0.76). The sensitivity and specificity of Q-CRT to predict sepsis are 0.72 and 0.81, respectively.[36]

Blood lactate level and CRT of end-organ perfusion were assessed in patients with sepsis admitted to the intensive care unit during the ANDROMEDA-SHOCK randomized clinical trial.[54] Although this was intended to monitor therapeutic interventions in sepsis, both measures improved dynamically in patients receiving active sepsis treatment. The findings indicated that directing resuscitation procedures using CRT resulted in lower rates of morbidity and mortality compared with resuscitation guided by serial lactate levels. According to some studies, tissue hypoperfusion is crucial to the sepsis process as shown by the mortality rate of up to 50% in individuals whose CRT did not normalize after sepsis therapy.[55,56]

Q-CRT is useful in various clinical settings. Yamamoto *et al*.,[33] for example, looked at the relationship between Q-CRT levels and postoperative outcomes in liver transplant recipients. The results showed that prolonged Q-CRT at ICU admission was associated with longer ICU and hospital stays, as well as an increase in postoperative sequelae. Similarly, Yasufumi *et al*.[36] investigated the predictive value of Q-CRT for sepsis in emergency department patients with suspected infections. The study results indicated that Q-CRT, when paired with the fast Sequential Organ Failure Assessment (qSOFA) score, improved the sensitivity and specificity of sepsis identification, comparable to recognized markers such as lactate levels.

In a pilot study by Morimura *et al*., Q-CRT was found to correlate with arterial blood lactate levels in ICU patients (Spearman's rank correlation coefficient = 0.681, $p < 0.001$).[30] The blood lactate level is used as an important indicator of low tissue perfusion and shock but is an invasive measure because it requires blood analysis.[57] Q-CRT would be a non-invasive, fast, and simple surrogate index. However, its applicability needs to be studied more thoroughly since no correlation between Q-CRT and blood lactate levels has been observed in patients admitted to the ICU before liver transplantation.[35]

Mrgan *et al*.[58] conducted a prospective observational cohort study to evaluate the correlation between CRT and short-term mortality, performing a multivariable analysis while considering age, sex, mean blood pressure, pulse, temperature, and peripheral oxygen saturation, the researchers discovered that higher CRT, both as a continuous variable and based on the Schriger and Baraff definition, was linked to a higher risk of death. Both the Trauma score and Schriger and Baraff criteria had substantial negative predictive values.

Recently, Sheridan *et al*.[59] detailed a novel technology that has been created using a problem-based innovation strategy to enable clinicians to rapidly assess CRT of end-organ perfusion at the bedside and be integrated into the electronic medical record. They emphasize the substantial benefits of this technology, such as the ability to enhance clinical outcomes without requiring substantial changes to clinical workflow or provider practice, the increased utility of this technology, and the use of reflected light technology for capillary refill assessment, which provides deeper tissue penetration with a lower signal-to-noise ratio than transmitted infrared light. The current device is primed for clinical research and is undergoing testing in both the ICU and ED to further validate its clinical evidence.[60]

Subsequent research conducted by the same authorsassessed the accuracy of a new medical device for measuring CRT. The device was compared to a rigorous manual technique and an unstructured conventional approach. Correlation coefficients using Pearson's method were calculated for 89 pairs of data. The Pearson correlation coefficient between the CRT measurements of the device and those of the research team was 0.693. The Pearson correlation coefficient between the provider CRT and the research workers CRT was 0.359. The findings showed significant potential in enhancing the evaluation of peripheral perfusion at the bedside during emergency department triage and during active resuscitation.

Kawaguchi *et al*.[61] developed a novel device that can be configured to measure CRT with precision by adjusting the pressing strength and time. The device was equipped with an electric actuator, color sensors, and strength sensors. Their findings indicated that a pressing time of 2 s was an effective threshold for obtaining sustained CRT measurements, and the optimal strength range was 3-7 N.

In addition to the various uses of Q-CRT in emergency medicine, there are promising studies on its application in dermatology.[22,62] It is argued that Q-CRT may add a new dimension to capillary function testing and the ultimate clinical outcome in patients with skin diseases and comorbidities.

Machine learning (ML) denotes computing algorithms engineered to derive insights or predictions from patterns inside data.[63-65] Statistical models designed to predict mortality in pediatric intensive care units in developed nations exhibit inconsistent efficacy in low- and middle-income countries, with the authors positing those disparities in patient characteristics and case mix account for these differences.[66] Pienaar *et al*. conducted internal validation of ML models for identifying severely unwell hospitalized children using a limited sample of novel data.[67] Models, including CRT, were assessed regarding discrimination, calibration, decision curve analysis, and SHapley Additive exPlanations (SHAP) analysis. All models exhibited adequate discriminatory performance in internal validation, aligning closely with the results from cross-validation in the development research.

5. Conclusion and perspectives

This study highlights the role of capillary refill time as a clinical indicator for assessing peripheral perfusion status. Our findings demonstrate that the Q-CRT technique represents a significant advancement in the evaluation of peripheral circulation and offers a more reliable and accurate alternative to traditional manual CRT measurements. Q-CRT is assessed using the principles of infrared and polarized spectroscopy. Blood is pushed back from the fingertip or other anatomical sites by controlled pressure application and the time required for the transmitted light intensity to return to 90% of its original value after the release of pressure is defined as Q-CRT. Similar to manual CRT assessment, Q-CRT can be affected by timing, skin site, temperature, gender, and age. However, for Q-CRT, the influence of many factors on the measurement outcome is reduced or eliminated (light conditions, intensity of applied pressure, subjective definition of when to stop time collection).

Future research should focus on improving the precision and reliability of Q-CRT measurements. New technologies, such as digital videography, 3D scanning, photogrammetry or modified oxygen saturation instruments, may be employed to achieve advanced CRT measurement in the future. These methods could eliminate the constraints associated with clinical CRT measurement and may even be capable of providing an automated CRT measurement. In addition to hardware enhancements that mitigate the modeled error, software enhancements are also required, including a straightforward method for subtracting the modeled error from the measured values and a correction method that accurately accounts for general modeled errors. Furthermore, more research is needed to evaluate the extent to which spectroscopy-based Q-CRT can substantially improve measurement quality, taking into account the technical, personal, and clinical factors influencing CRT. Therefore, the practical application of Q-CRT demands the further refinement of protocols, interpretation of algorithms, and resulting outcomes. Finally, more studies are needed to clarify the mechanisms of association between Q-CRT values and postoperative outcomes in various clinical scenarios.

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Conflict of Interest

There is no conflict of interest.

Supporting Information

Not applicable.

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