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ORIGINAL ARTICLE

Intra-operative Video Characterization of Carotid Artery Pulsation Patterns in Case Series with Post-endarterectomy Hypertension and Hyperperfusion Syndrome

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Abstract

Cerebral hyperperfusion syndrome (CHS) is a complication that can occur after carotid endarterectomy (CEA), the treatment of choice to decrease the subsequent risk of fatal or disabling stroke for patients with symptomatic severe stenosis of the carotid artery. Because of its rarity and complexity, the mechanism of the condition is still unclear, making its prevention via prediction and monitoring challenging. This is especially true during surgery, when multiple factors can induce physiological changes, including blood pressure and baroreceptor functions, which are crucial factors for post-CEA hypertension and CHS. Thus, with intra-operative videos taken by surgical microscopes, we employed a new video processing technique to magnify ordinarily invisible carotid artery pulsation patterns as rhythmic color fluctuations. We applied the technique for three CEA cases, two of which developed CHS with post-CEA hypertension. For those with CHS, abnormal pulsation patterns were detected at the site of the baroreceptors. The results suggested that intra-operative baroreceptor dysfunction can potentially be linked with post-operative hypertension, as well as the occurrence of CHS. Guided by the preliminary discovery, further investigation may help establish the introduced technique as a simple and contactless technique to help predict post-CEA hypertension and CHS in order to facilitate the management and understanding of the condition and improve the care of CEA.

Keywords Carotid endarterectomy · Image processing · Surgical video · Cerebral hyperperfusion syndrome · Baroreceptor · Hypertension

Introduction

Carotid endarterectomy (CEA) is currently the treatment of choice to decrease the subsequent risk of fatal or disabling stroke for patients with symptomatic severe stenosis of the carotid artery. One complication that can occur after the procedure is cerebral hyperperfusion syndrome (CHS). The condition is defined as severe unilateral post-operative headache ipsilateral to the site of endarterectomy, seizures, or even stroke, accompanied by increased ipsilateral internal carotid artery (ICA) volume flow (> 100%) compared with intraoperative values and no evidences of new cerebral ischemia, post-operative carotid occlusion, and metabolic or pharmacologic cause. In general, CHS can occur any time during the first 28 days post-operatively [1], but most studies reported onset CHS within several hours to several days. With a cited incidence of below 3% in most literature [2], CHS is a relatively rare condition.

Due to its rarity, the mechanism of the CHS is still not well understood, and can be subject to many interlinked factors. First, impaired autoregulation weakens the reactivity towards increased cerebral blood flow after CEA, and thus can result in fluctuations in blood pressure (BP), post-operative hypertension, increase in cerebral perfusion pressure (CPP), and risk for intracerebral hemorrhage (ICH) in hypoperfused tissues,

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as well as transient bradycardia and cerebral blood flow (CBF) changes [3]. The autoregulation system can be influenced by chemicals, such as nitric oxide [4] and oxygen-derived free radicals produced during CEA [5]. A second factor that may be associated with CHS is baroreceptor dysfunction, which results in progressive increase of blood pressure post-operatively. Surgery to carotid arteries is linked to baroreceptor dysfunction, and baroreceptor denervation has been reported after CEA, especially after successive bilateral CEA leading to CHS [6, 7]. In addition to the direct impacts of surgery, including physical trauma, several other factors also contribute to baroreflex dysfunction, including chronic hypertension, carotid artery disease, diabetes [8], the effects of antihypertensive medication [9], recent transient ischemic attack (TIA) or stroke [10, 11], and the effects of age [12]. Lastly, pre-operative chronic hypertension is another factor, which leads to endothelial dysfunction and micro-angiopathy. These can in turn result in blood-brain barrier (BBB) damage that induces cerebral edema and seizure-like activity in patients with no prior edema [13]. In general, there are a large number of risk factors to take into consideration [2, 3, 7], which can be categorized in perioperative blood flow changes due to surgical procedures, preoperative circulation issues, and drug administration. Majority of them impact the blood pressure of the cardiovascular system to influence the development of CHS, but much remained to be studied. For more thorough summaries and discussions of these factors, the readers can refer to [2, 3, 7].

Although most patients have mild symptoms from CHS, progression to severe and life-threatening symptoms can occur if CHS is not diagnosed and treated in time and adequately. Unfortunately, so far, no consensus has been achieved on an effective technique to predict CHS, especially intra-operatively, when various factors may change the physiological states (e.g., baroreceptor functions) of the patient that can induce CHS. Recent developments in signal processing techniques [14, 15] have allowed us to effectively magnify subtle dynamic information, such as tiny motions and color changes captured in video footages. From biological video recordings, this may offer us richer insights about the body that are usually hidden from the visual capacity of the naked eyes. For example, the technique has been used to visualize the blood flow of the human face with videos taken by a conventional digital camera [14, 15]. To inspect the state of the carotid artery during CEA, we obtained intra-operative video footage of the surgical site before incision using a surgical microscope. From the processed videos, we have observed incoherent blood pulsation patterns at the site of the baroreceptors in comparison to the rest of the carotid artery for those with CHS. These preliminary observations potentially indicate that baroreceptor dysfunction may be linked to post-CEA hypertension and CHS.

In this article, we present our discovery as a case report on 3 CEA cases (2 with post-CEA CHS) and further discuss the phenomena's potential association with post-CEA hypertension and hyperperfusion syndrome, as well as revealing its possible role in predicting CHS for timely management of the condition.

Materials and Methods

Patients and Data Acquisition

To demonstrate the technique, we enrolled three patients who had severe carotid artery stenoses and underwent routine carotid endarterectomy. They were recruited prospectively for the study based on the sole criterion of developing post-CEA CHS, and CT perfusion was performed pre-operatively to assess the blood flow. All surgeries successfully removed the stenosis, and restoration of blood flow was confirmed by intra-operative Doppler ultrasound. Short video footages (30–40 s) of the carotid artery before incision for each patient were obtained through the surgical microscope and were later used for further image processing and data analysis. Informed consents were obtained from all patients, and the study was approved by the local ethics committees. Among the cases, two cases (Patients 1 and 2) were recruited at the Montreal Neurological Hospital (Montreal, Canada), and one case (Patient 3) was operated at the Tokyo Women's Medical University Medical Centre East (Tokyo, Japan). All patients had more than 75% stenosis. The regions of stenoses are shown in Fig. 1 for all cases. While Patient 1 showed no signs of CHS, both Patients 2 and 3 have developed CHS after CEA. More specifically, Patient 1 was a 75-year-old male with TIA and numbness in the right hand, and his pre- and post-operative systolic blood pressures (SBP) were measured at 130–160 mmHg. Patient 2 was a 61-year-old hypertensive and dyslipidemic male with diabetes. Five days after surgery, the patient experienced hypertension, with headaches as manifestation of reperfusion syndrome (SBP = 160–190 mmHg), which was confirmed by CT perfusion imaging, and later resolved with blood pressure control. Patient 3 was a 76-year-old male who was presented with recurrent episode of right frontal convexity embolic infarction secondary to severe carotid stenosis. After CEA, the patient developed cerebral hypertension syndrome as documented on Day 1 with a SBP above 180 mmHg post-operatively, requiring sedation and blood pressure control, and evidence of hyperperfusion was confirmed by CT perfusion imaging. The patient also manifested with an epileptic seizure, which was treated with anti-epileptic therapy.

Video Magnification

To reveal hidden blood flow patterns within the carotid arteries during surgery, we used two different video magnification

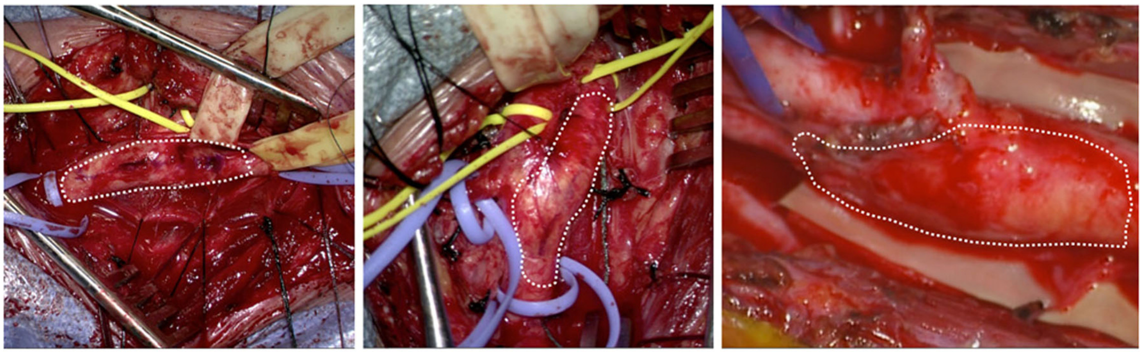

Fig. 1 Regions of stenoses as contoured with white dotted lines for Patients 1, 2, and 3

methods introduced in [15] and [14] in conjunction, and generally speaking, both methods can amplify the temporal information through three steps. First, the video footage is decomposed into multiple spatial frequency components that encode the dynamic changes (i.e., motion or color) at different speeds. Then, the target frequency component to be enhanced is multiplied by a desired factor of α. Finally, the enhanced video can be reconstructed by re-combining all the frequency components together. While magnification can be achieved with the selection of $\alpha>1$, reduction or attenuation can also be performed when $\alpha<1$. Comparing between the two methods, enhancement of dynamic color changes can be better obtained with Eulerian Video Magnification [15], while the more recent phase-based video processing technique [14] performs better in motion magnification or attenuation.

Video Processing

Short video footages (10 s in the mid-section of the entire video) were obtained with the neurosurgical microscope during the surgery from three patients. This way, we ensure that the video footages do not contain moving surgical tools and camera motions that typically occur at the beginning and end of the videos. The video sequences were processed in two steps. First, to facilitate the blood flow assessment, arterial pulsations in the videos were attenuated with a phase-based video enhancement method [14]. Then, the dynamic image intensity changes between the frequencies of 0.5–2 Hz were magnified by a factor of 150 using Eulerian Video Magnification [15]. The same magnification factor of 150 was applied to all patients and was determined by visual inspection. We expect the same magnification factor to work for larger trials. The theories and algorithms of the video processing techniques are detailed in [14, 15]. As the normal human heart rate is around 60–100 bpm (1–1.67 Hz), the range of 0.5–2 Hz will capture a wide range of possible pulsation frequencies, and the precise frequency for a particular patient can be found with power spectral analysis.

Bio-signal Analysis

Regions of interest (ROIs) were manually selected from motion-attenuated video footages based on visual inspection of blood flow patterns uncovered from video magnification. More specifically, for Patients 2 and 3, the boundary of reversed color changes at the site of baroreceptor (ROI2 in Figs. 3 and 4) in contrast to the rest of the carotid artery can be easily contoured by visual inspection. The rest of the ROIs were contoured for the remaining exposed regions in different branches of the arteries. As for Patient 1, since there was no visible region of reversed color changes, the two ROIs were just two branches of the carotid artery. To quantitatively evaluate the uncovered patterns, Signals (RGB converted to greyscale) were averaged within these selected regions to observe the effects, and plotted against the time. In addition, the pulsation rates of different regions were computed through power spectral analysis, and the values were taken at the frequencies with the largest magnitudes.

Results

The results of processed videos for the three patients are shown in Figs. 2, 3 and 4, along with the selected regions of interest for analysis. Note that the blue rubber bands were tied very loosely around the artery to help identify and secure it in place, and no physical manipulation was made on the artery when the video was taken. In the original video footages, simple visual inspection of the carotid arteries detected no periodic color alternations due to blood pulsation, and no particular differences were found across all three patients. However, from the enhanced videos, the arteries showed periodic color fluctuations, generally alternating between pale pink and dark red. Additionally, the differences in the dynamic color patterns of the carotid arteries, as surrogates for blood flow patterns, between Patient 1 and the rest of the patients were evident. For Patient 1, the blood flow appeared coherent for the entire carotid artery, but for Patients 2 and 3, the blood

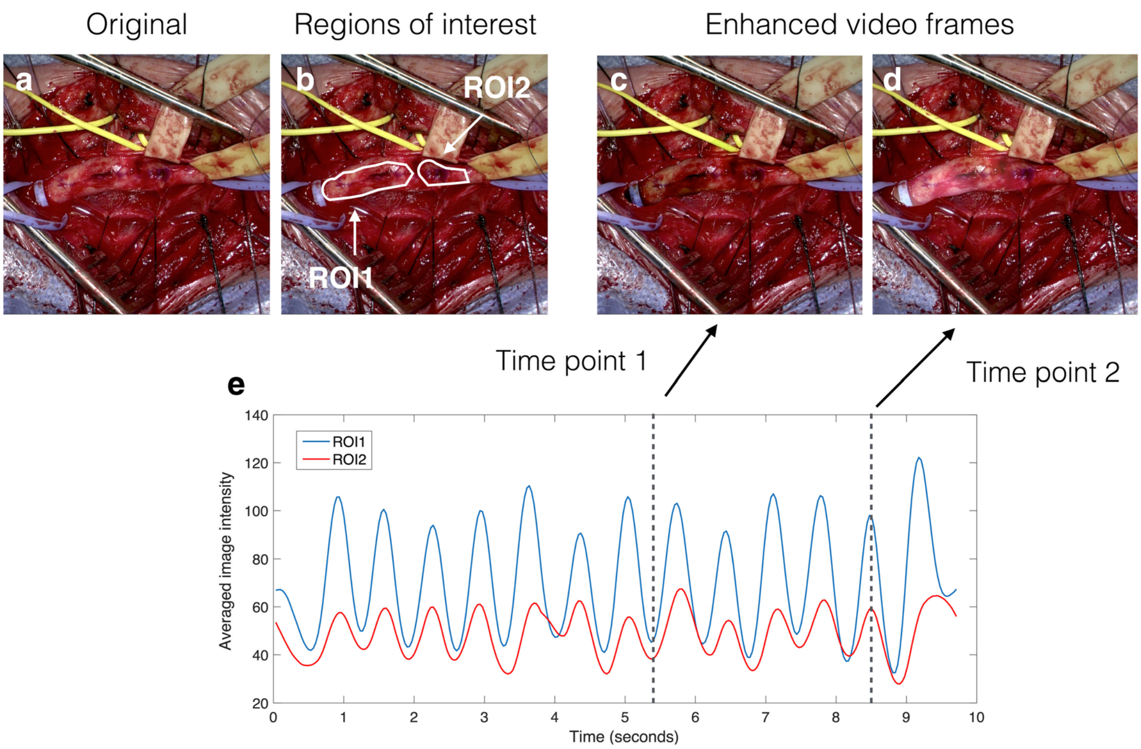

Fig. 2 Video enhancement results for Patient 1. **a** Original video footage. **b**: Demonstration of regions of interest (ROIs). **c** and **d** Frames at time points 1 and 2 from the enhanced video footage. **e** Averaged image intensities within the ROIs plotted with respect to time

flow at the site of the baroreceptor (ROI2 in Fig. 3b and 4b) was in reverse trend of the rest of the carotid artery. To better depict the difference, the temporal changes of image intensities in the selected regions were plotted in Figs. 2, 3, and 4 for Patients 1, 2, and 3, respectively. Through power spectral analysis, the blood pulsation rates across all ROIs

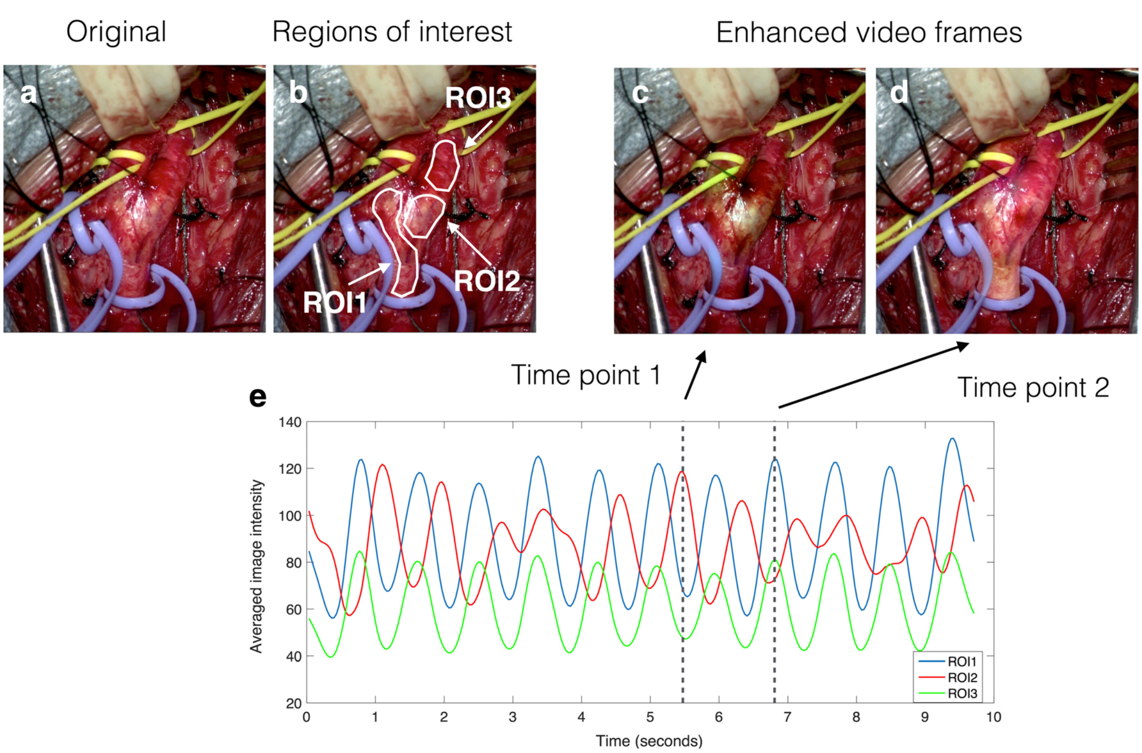

Fig. 3 Video enhancement results for Patient 2. **a** Original video footage. **b** Demonstration of regions of interest (ROIs). **c** and **d** Frames at time points 1 and 2 from the enhanced video footage. **e** Averaged image intensities within the ROIs plotted with respect to time

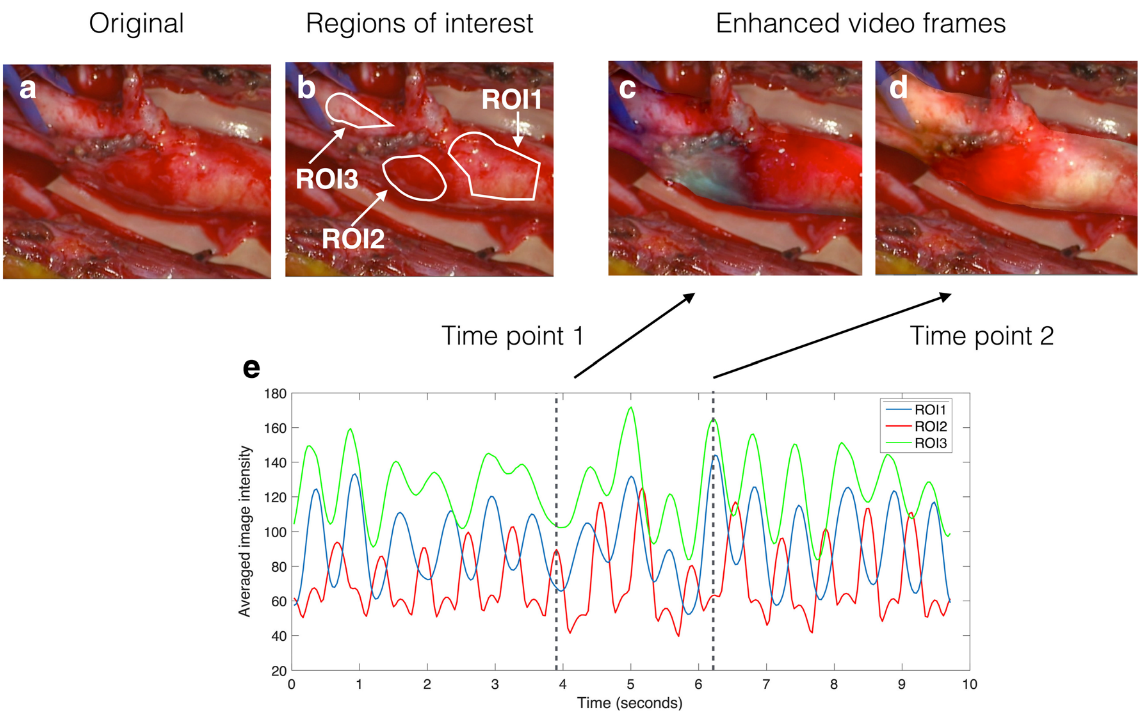

Fig. 4 Video enhancement results for Patient 3. **a** Original video footage. **b** Demonstration of regions of interest (ROIs). **c** and **d** Frames at time points 1 and 2 from the enhanced video footage. **e** Averaged image intensities within the ROIs plotted with respect to time

were the same for each patient. More specifically, the blood pulsation rates for Patients 1, 2, and 3 were measured at 1.44 Hz (86.4 bpm), 1.13 Hz (67.8 bpm), and 1.545 Hz (92.7 bpm), respectively.

Discussion

We employed image processing techniques [14, 15] to uncover the dynamic bio-signals of the intact carotid artery during carotid endarterectomy. As a result of blood pulsation, in the processed videos, the artery displayed periodic color fluctuations, which were not perceivable in the original video recordings. This is consistent with the previous observation when using the same technique to monitor blood pulsation rate from video footages of the human faces [14, 15]. Since the arterial wall has certain level of translucency, as oxygenated blood flows in, the relevant portion of the artery will appear redder, giving rise to the observation. When abnormal blood flow presents, color variations across different sections of the artery will appear. This could be the case for the reversed trend of color change at the site of baroreceptor, under which turbulent flow occurs as the baroreceptor fails to react to the blood pressure change. In addition to colors, subtle motions, such as arterial pulsation, can also be magnified and transformed into pulsation rates [15]. However, in the demonstrated application, the former offers richer insights. The arterial pulsation and blood flow pulsation are related, but not the same. The pulsation rates measured through the dynamic changes are for blood flow pulsations. For analysis, we only measured the pulsation rates as the magnitude of the signals in Figs 2, 3, and 4 did not offer any potential trend among the patients. This can be due to the fact that the magnitudes are often influenced by the camera properties and settings, but it remains an interest of future investigation.

There are two main perspectives of our observation and measurements. First, at the site of the baroreceptor in the enhanced videos, the periodic color fluctuations are in reverse trend as the rest of the carotid artery for those with post-CEA CHS. This may imply that for those who developed CHS, their carotid baroreceptors failed to regulate blood pressure homeostasis with the presence of stenosis, and as mentioned earlier, baroreceptor dysfunction may be linked to post-CEA hypertension and CHS. It is known that lower pre-operative baroreceptor sensitivity is more common among patients that require treatments for post-CEA hypertension [16], and the sensitivity of the baroreceptor can be altered with various diseases, such as chronic hypertension, carotid artery diseases, and cerebrovascular diseases. Carotid baroreceptor denervation can be induced from the surgical procedure as a consequence of sudden blood pressure change after removing the stenosis or possible physical damage from incision [17]. For the first cause, the introduced technique may help reveal the state of the baroreceptor intra-operatively, but techniques that precisely quantify the level of sensitivity will require further exploration with more data. As for preventing possible physical injury of the baroreceptor, the introduced technique may help identify the region under the influence of the baroreceptor during surgery, avoiding the possible physical damage, especially considering recognition of carotid baroreceptors with visual inspection is challenging and the relevant region can vary across patients. The second perspective lies in the pulsation rates. Both Patients 1 and 3 had elevated pulsation rates compared with Patient 2, and no trend was directly clear in terms of CHS development. Unfortunately, due to the limited cohort, it is not feasible to statistically analyze the relationship between pulsation rates and CHS, and between pulsation rates and blood pressure. It is important to note that for both perspectives revealed by the enhanced videos, they reflect the states of the carotid arteries at the time during the surgery, and a number of pre-operative and intra-operative factors may have collectively contributed to the observations. As the recent study [18] confirmed that impaired baroreceptor sensitivity and poorly controlled blood pressure measured pre-operatively are strong indicators of post-CEA hypertension, and enhance CHS, the proposed technique may provide the necessary insights into these factors in the intra-operative state that are can altered by multiple factors during surgery.

At the moment, the diagnosis of CHS is primarily based on non-specific criteria. Patients may be misdiagnosed as having one of the better-known causes of perioperative complications like thromboembolism. The ensemble of perioperative risk factors can on some level provide supports for the diagnosis, but relevant factors with respect to each individual are often complex to pinpoint, difficult to quantify, and subject to changes under the interplay of various influences. In the clinic, Doppler ultrasound can be used to help monitor the blood pulsation intra-operatively [19–21]. However, the technique requires direct contact and can be cumbersome. The introduced technique requires only very short intra-operative video recordings of the carotid artery, which can be obtained with a surgical microscope that is integrated in the surgical workflow, or even a phone camera. Thus, the physiological information can be acquired without direct contact. In addition, the graphic information regarding the irregular baroreceptor function can be further processed and digitally augmented to the microscopic view as augmented reality to facilitate the decision on the extent of incision.

In this case study, we recruited three cases with two who developed CHS with hypertension after surgery, and the preliminary results suggest the association between the observations from the recovered bio-signals to post-operative hypertension and CHS. Due to the rarity of CHS, one limitation of this study is the small patient cohort. Thus, it is difficult to establish a statistical model to quantify the observations and measurements from the enhanced videos in regard to the known risk factors and the individual-based symptoms of CHS. In the near future, we will further confirm the association between the observations from the enhanced videos and CHS with a large cohort of patients, which will potentially help us build a computational model to better understand and hopefully predict post-CEA CHS.

Conclusion

In this article, blood pulsation patterns of the carotid artery were visualized and characterized by magnifying color fluctuations of the artery seen in video footages during carotid endarterectomy. Preliminary results from three CEA cases have revealed incoherent patterns at the site of baroreceptor from the rest of the carotid artery for those who suffered from hypertension and CHS following the procedure. We postulate that the observation is a result of baroreceptor dysfunction in the intra-operative state and can be used to help predict the occurrence of post-CEA hypertension and CHS. With further investigation, the simple and contactless technique has the potential to offer a convenient biomarker to detect post-CEA hypertension and CHS, greatly benefiting the management of the condition especially during and after surgery.

Compliance with Ethical Standards

Conflicts of Interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all participants included in the study.

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