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OTOLOGY

Microcirculation evaluation of facial nerve palsy using laser speckle contrast imaging: a prospective study

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Abstract

Objective Facial nerve palsy (FNP) is a common disease in the otorhinolaryngological department. Besides the main symptom of motionlessness occurring in the ipsilateral facial muscles in FNP, there are other common complaints of numbness, stiffness and tightness in ipsilateral face described by the patients. Based on our pilot study, we further investigated the relevance between these complaints and facial microcirculation.

Method Function of facial microcirculation was evaluated by laser speckle contrast imaging (LCSI). Facial perfusion was measured in 143 patients with facial nerve palsy (FNP) at the first visit and follow-up visit under the same conditions.

Results Difference in FNP patients' facial microvascular perfusions between ipsilateral and contralateral side was significant ($P = 0.0002613$). Facial perfusion of patients with Bell's palsy ($P = 00089$) and facial nerve tumors ($P = 0.025110$) was significantly decreasing in the ipsilateral side. Improvement of perfusion could be seen after treatment.

Conclusion A positive correlation of FNP severity and microvascular impairment can be noticed. During treatment, patients' ipsilateral perfusion could increase. Therefore, this objective method can measure ipsilateral perfusion in the patients with FNP and the ipsilateral microvascular impairment can be detected through this method.

Keywords Otology · Facial nerve · Facial palsy · Cholesteatoma

Introduction

Facial nerve palsy (FNP) is a common disease in the otorhinolaryngological department, which can be triggered by Bell's palsy, Ramsay Hunt syndrome, Melkersson–Rosenthal syndrome, trauma, tumors, or a middle ear infection. Besides the main symptom of motionlessness occurring in the ipsilateral facial muscles in FNP, there are other common complaints of numbness, stiffness and tightness in ipsilateral face described by the patients. To date, there has been little attention given to and agreement on the assessment method and mechanism of this complaint.

Because of the microcirculation which has been recognized as having a relationship with the sensations of superficial skin, we assume that it is the microvascular dysfunction that leads to the numbness and tightness in the FNP patients. Currently, a variety of non-invasive techniques has been developed to examine the skin microcirculation. Compared to widely used laser Doppler flowmetry (LDF) and laser Doppler imaging (LDI), laser speckle contrast imaging (LSCI) is capable of measuring perfusion in an area within a low amount of time while providing high temporal and spatial resolution, which makes it a promising tool that has been increasingly used in the past few years. LSCI is performed depending on an interference pattern generated by reflecting or scattering of light by moving red blood cells from different parts of the illuminated surface [1, 2]. According to the mechanism, LSCI is practical since it can obtain images of blood flow in a range of situations such as burn depth assessment, wound healing, cardiac activity analysis, Raynaud's phenomenon and others non-invasively [3]. However, the

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applications of assessing the microvascular function have not been performed in the facial nerve palsy patients. Therefore, the aim of this study was to introduce an application of LSCI in the FNP patients to investigate how the perfusion amid FNP patients changes and consider the feasibility of LSCI as a measurement of the severity and prognosis of FNP.

In our pilot study, to set up the appropriate measurement and the right locations to measure, we analyzed 20 normal volunteers. We performed the measurement once every 2 weeks to obtain the normal range in the volunteer. No significant differences ($P > 0.05$) were revealed between the microvascular perfusions on both sides of the face. We also selected the following areas as our regions of interest (ROI) measuring perfusions in the pilot study, the areas around eyes, areas of nasolabial groove, areas of angulus oris and cheek. The reason why we chose these sites was that they were the main areas where the facial nerve and its branches go around. The result showed that there was no significant difference between the perfusions in ipsilateral side and contralateral side in the area of nasolabial groove, angulus oris and cheek. On the contrast, difference between both sides of the area around the eyes in the FNP patients has been revealed ($P < 0.05$). Consequently, we selected to measure the perfusions of areas around eyes in the following FNP patients. Moreover, from this pilot study, the perfusion's normal range is uncertain due to the great fluctuation between the subjects.

Patients and method

Laser speckle contrast image

LSCI is a contactless technique which could reveal microvascular blood flow maps based on the optical principle. It applies a 785 nm laser to light the sample creating a speckle pattern and detects the speckle pattern using a low frame rate CCD camera. To indicate the fluctuating sample, a relating speckle contrast across a 5*5 or 7*7 pixel array can be used to calculate and build an appropriate model of blood flow. Based on this mechanism, blood perfusion is expressed in arbitrary units [4]. Compared to laser Doppler, LSCI is with more sensitivity to movement articles.

Apparatus and procedures

All microvascular measurements were performed in the same consulting room under natural light condition with room temperature 23 ± 1 C and 40–60% humidity by the same medical technologist. Each subject was demanded to stay comfortably for 15 min before measurement. Microvascular function measurements, image analysis and data recordings were performed using the PeriCam PSI System, a blood perfusion imager based on Laser Speckle Contrast Analysis (LASCA) technology (PeriCam PSI system, Perimed, Järfälla, Sweden). The equipment in our department is shown in Fig. 1. After the calibration was completed, we performed 1 min measurement of the cutaneous basal blood flow and selected a 12 cm × 12 cm area around the eye on each side of the skin as ROI to collect its data of perfusion. During the measurement, subjects were requested to lie down on the same examination bed and remain supine. The distance between the laser head and the skin surface was fixed at (15 ± 1) cm, since it has been reported that the distance between 10 and 30 cm would not have an impact on the skin blood flow recordings at rest or at peak's microvascular responses [5].

Patients' selection

Eligible subjects were selected at the Department of Otolaryngology in Beijing Electric Power Hospital. Entry criteria were patients with unilateral facial nerve palsy. On the other hand, patients who were suffering from facial skin lesions or with bilateral facial nerve palsy were excluded. All subjects were informed about the measurement and the use of their data. They all endorsed the agreement. This research was conducted in conformity with the Declaration of Helsinki and was approved by the institutional ethics committee of Beijing Electric Power Hospital.

Fig. 1 The equipment of laser speckle contrast imaging

Sunnybrook Grading System

We used the Sunnybrook scale to assess the severity of FNP and detect the changes of a patient's motor recovery, tone, synkinesis and symmetry. The scale refers rating of symmetry of the eye, cheek, and mouth at rest and movement during five standard facial expressions.

Statistical analysis

Data were summarized by counts and percentages for categorical variables, and means and standard deviations for continuous variables. Perfusion was summarized by means and standard deviations.

The variance of perfusion (ΔP) on both sides of the face was calculated by subtracting the perfusion of ipsilateral side from that of contralateral side for each participant.

$$\Delta Pi = Pi(\text{ipsilateral}) - Pi(\text{contralateral}) \quad (i = 1, 2, \ldots, 143)$$

Besides, we calculated the variance rate between the two sides of face to evaluate the extent of microvascular malfunction. The rate of change was set as ΔP/perfusion of contralateral side.

$$\Delta Pi\% = \Delta Pi / Pi(\text{contralateral}) \quad (i = 1, 2, \ldots, 143)$$

We keep the sign to indicate the trend of change in the ipsilateral perfusion which can be increasing or decreasing.

Paired *t* test and Wilcoxon signed-rank test were used to compare the two sides. The statistical significance was considered at a probability of $p < 0.05$ level. All statistical analyses were performed using IBM SPSS Statistics for Mac, Version 22.0. The statistical package was Prism version 6.0 (GraphPad Software Inc. La Jolla, CA, USA).

Results

Patient characteristics

In the first visit, 143 patients (66 males, mean age 40.987 ± 13.9033 years; 77 females, mean age 36.106 ± 12.2149) with unilateral facial nerve palsy (57 Bell's palsy ; 32 Ramsay Hunt palsy; 23 Melkersson–Rosenthal syndrome; 12 tumor; 10 trauma; 7 otitis and cholesteatoma; 2 congenital facial palsy) were enrolled from March 2016 through July 2017. The etiologies of the subjects are shown in Fig. 2. No patient was excluded from the analysis. Measurements of facial microvascular perfusions were implemented before receiving treatments from our department, 2 months, 4 months and 6 months after our treatments began. However, several subjects dropped out of our study during the follow-up period. A specific result of the exam is displayed in Fig. 3. In Fig. 3, the left diagram shows the change of microvascular perfusion quantity within a period of time. The right picture shows one of the subjects' speckle image during the exam.

During 143 patients' first visits to our department before receiving our treatments, we found that the difference in perfusions of areas around eyes between ipsilateral side and contralateral side was significant ($P < 0.0001$). No influence of sex was noted among the patients between the perfusions of both sides. The results also showed no difference between the variance of perfusions and the specific side (left or right side).

Perfusions in different causes

We considered how perfusions changed between different causes of FNP. In the study, among the patients with Bell's palsy and facial nerve tumors on their first visits, the difference between the perfusions in the areas around the eyes on both sides was significant, whereas differences among the patients with Ramsay Hunt, Melkersson–Rosenthal

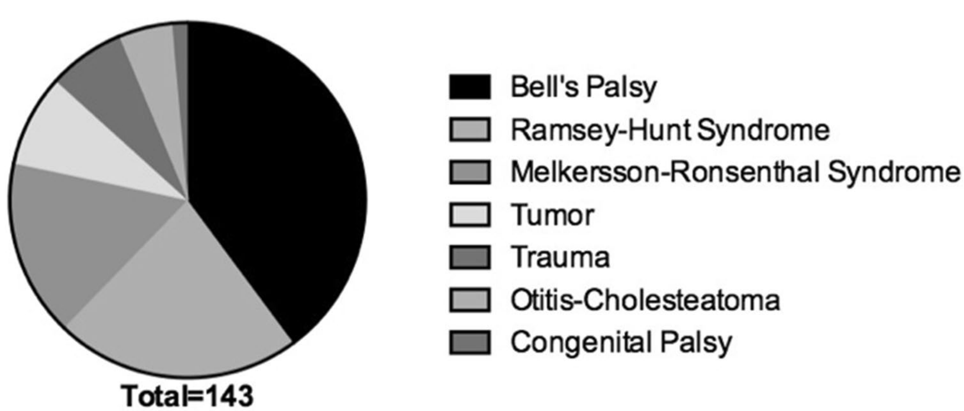

Fig. 2 Etiology of FNP in study patients ($n = 143$)

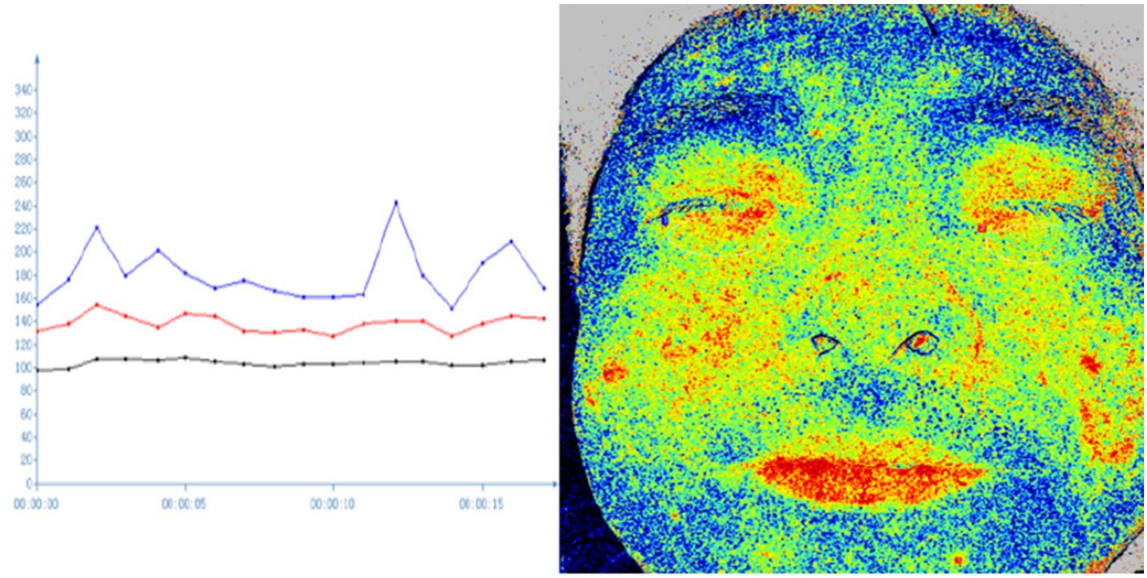

Fig. 3 A patient's facial perfusion

syndromes and trauma were observed, but it did not reach statistical significance. Meanwhile, we did not refer the comparisons among patients with middle ear infection and congenital palsy owing to their restricted sample sizes. We calculated ΔPi% of each cause, the results are shown in Table 1 and Fig. 4. It is noticeable that Bell's palsy and Ramsay Hunt groups have smaller change rate ranges below the baseline, which indicates the significant differences of perfusion in the two groups. Oppositely, other groups have larger ranges which are even beyond the baseline. Correspondingly, it means the ipsilateral perfusion could be higher than the other side.

Perfusions in different onset time

Based on the pathological changes during the FNP process, we classified the patients into four groups based on their onset time: acute phase group (onset time ≤ 1 month), subacute phase group (1 < onset time ≤ 2 months), chronic phase group (onset time > 2 months) and recurrent group. We found that the differences between the two sides of face were statistically significant in each group ($P < 0.0001$). Accordingly, the perfusion in ipsilateral side is decreasing before carrying out effective treatments. The change rates of the three groups are illustrated in Fig. 5. What draws our attention is that the acute group has a greater fluctuation compared with the other groups.

Perfusions in different Sunnybrook scores

We grouped the subjects in the first visit according to their Sunnybrook scores. Group I: 0 ≤ scores < 25; Group II: 25 ≤ scores < 50; Group III: 50 ≤ scores < 75; Group IV: 75 ≤ scores < 100. We calculated each group's mean value and standard deviation. The results are depicted in Fig. 6. The change rate (ΔPi%) is higher at a worse FNP stage, as a result a positive correlation between FNP severity and microvascular impairment can be noticed.

Perfusion's change after treatments

In our department, the major treatments of FNP are medical management and surgery. We choose the proper treatment for each FNP patient based on each one's history and

Table 1 Characteristics of patients

	Bell's palsy	Ramsay Hunt	Melkersson–Rosenthal syndrome	Trauma	Tumor	Total
Subjects	57	32	23	10	12	143
Ipsilateral	202.7339 ± 6.65396	211.9766 ± 10.81056	230.7939 ± 12.19591	221.0410 ± 20.10164	234.0050 ± 20.98787	213.5340 ± 4.79024
Contralateral	255.7237 ± 11.23964	262.1850 ± 13.19667	261.5204 ± 11.39392	234.0300 ± 22.05070	259.5233 ± 22.18049	255.0506 ± 6.28365
P	0.00089	0.000003	0.015439	0.628870	0.025110	0.0002613
ΔPi%	− 0.1669 ± 0.02858	− 0.17564 ± 0.027654	− 0.10198435 ± 0.047366985	0.01386834 ± 0.11688790	− 0.0897423 ± 0.45036680	− 0.12956217 ± 0.019671818

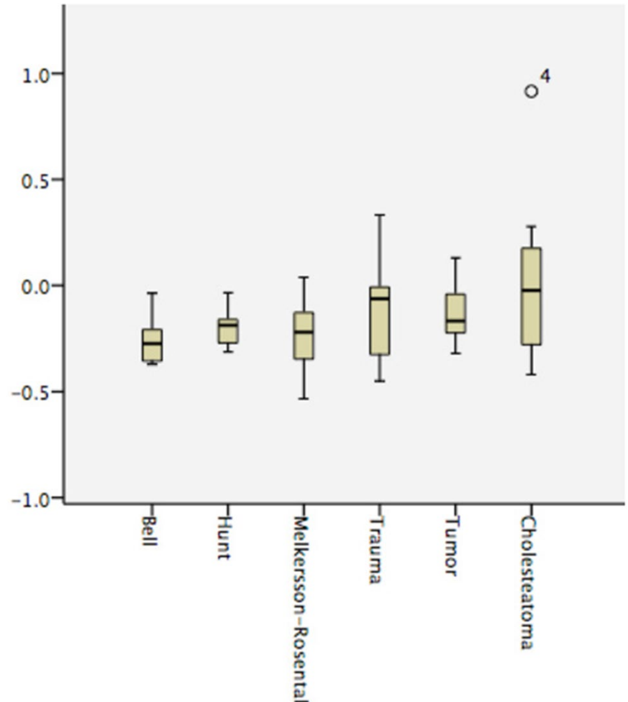

Fig. 4 Causes of patients

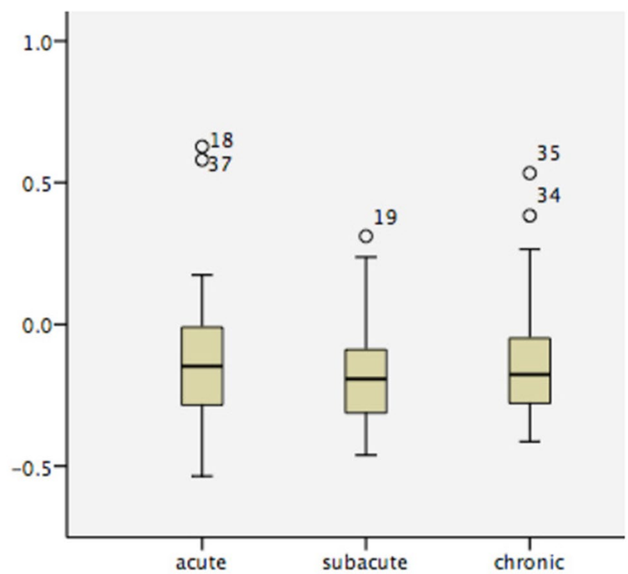

Fig. 5 Onset time of patients

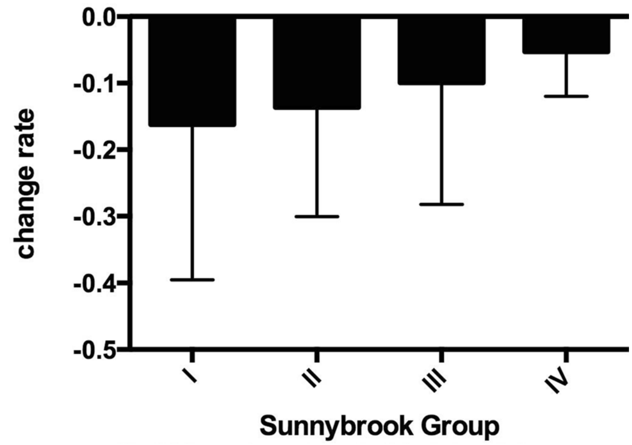

Fig. 6 Mean value and standard deviation of change rate according to Sunnybrook scores

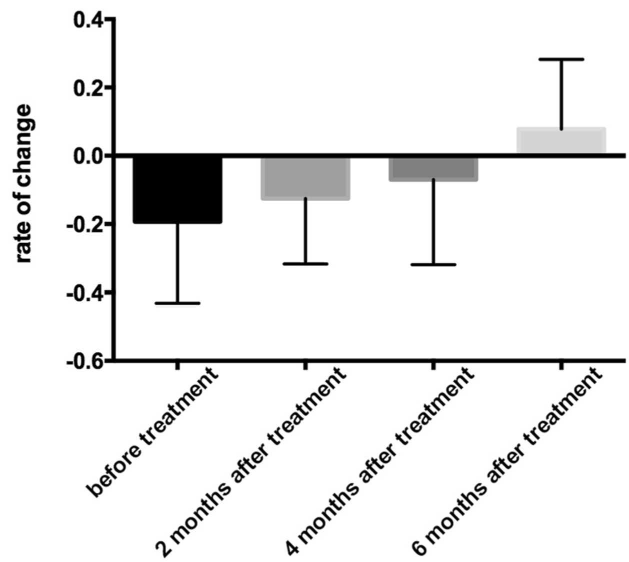

Fig. 7 Different treatment periods leading to different results

severity. Generally, we advise patients to return for a visit after about 2, 4, 6 months after treatments. During the follow-ups, the easiness of numbness, stiffness and tightness in ipsilateral face was conveyed from patients. We showed the change after treatments in Fig. 7. We analyzed the trend of perfusion variance, which revealed that the ipsilateral perfusion increased during the treatment. Moreover, the ipsilateral perfusion could surpass the contralateral perfusion after a 6-month treatment.

However, individual differences can be observed in the improvement of perfusion after treatments. While some subjects showed obvious and rapid improvements of perfusion, others tended to experience slow and inconspicuous improvents of perfusion. The mechanism of this difference needs to be further explored.

Perfusion change process

According to the histories of facial palsy, we selected subjects who will come to the hospital regularly for follow-up for a long period after taking our treatment and analyzed their variance rate of perfusions.

As shown in the results in Fig. 8, each thread represents a patient's ΔPi% change process. These six subjects were visiting regularly on average 1–3 months, 3–5 months, 5–7 months and 7–9 months after the first treatment in our department. Other than the overall trend of becoming better, no transparent rules of changing have been remarked. A subject's perfusion change tendency is illustrated in Fig. 9. The patient showed in Fig. 9 suffers right-side FNP. Perfusion image A is acquired before treatment and perfusion images B to F are acquired at 2 months, 4 months, 6 months, 8 months and 10 months after the treatment. These images indicate a trend of increasing perfusion in the face typically in the area around the right eye.

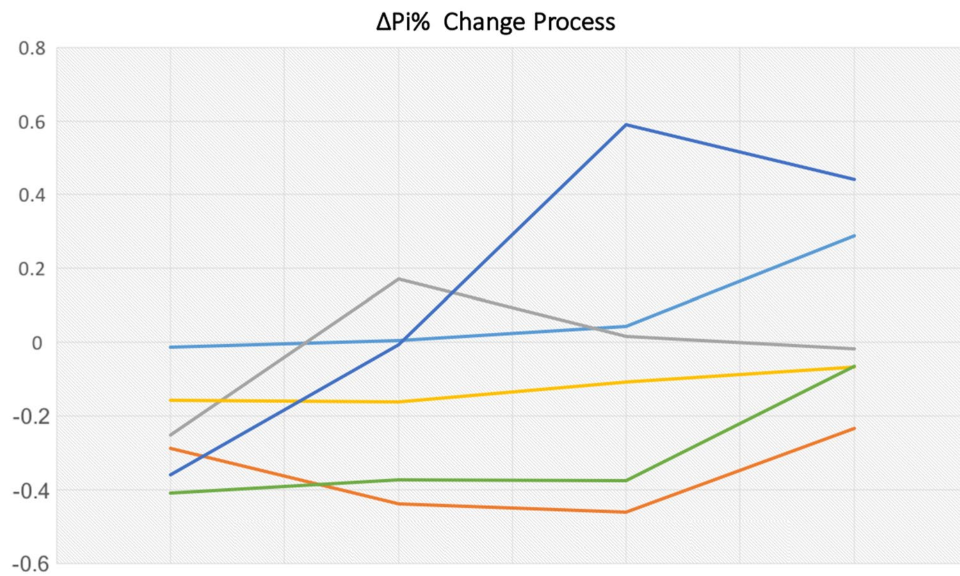

Fig. 8 Six patients' ΔPi% change trend

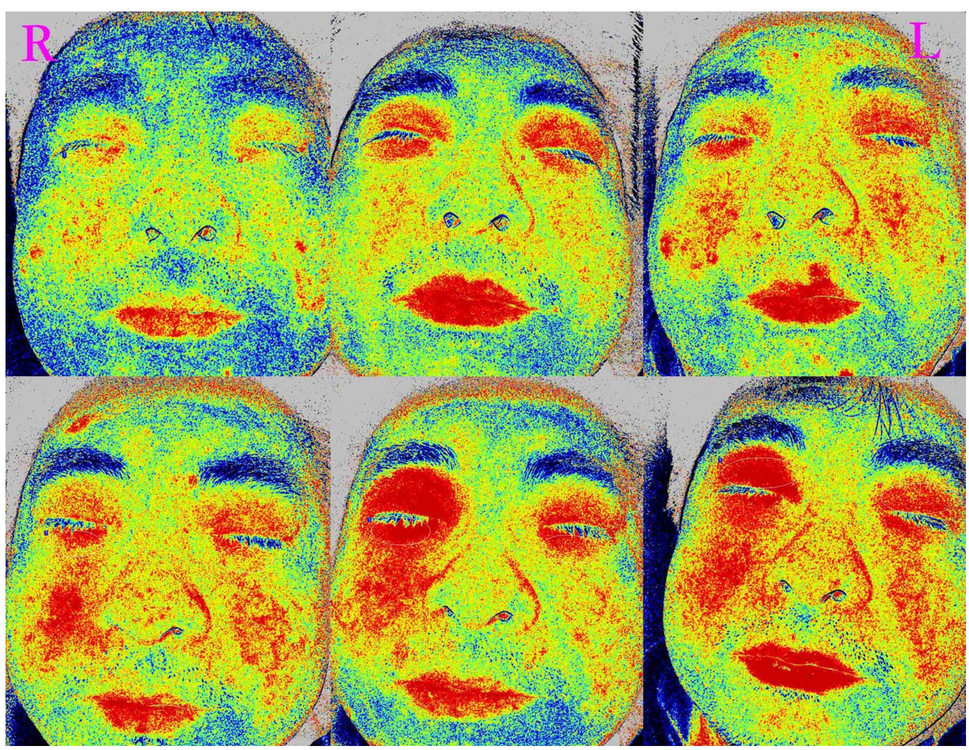

Fig. 9 A patient's perfusion in face in various time periods

Discussion

As a common disease in the ENT department, FNP can also generate an abnormal feeling of facial skin at the affected side. In this study, we found the correlation between FNP and change of microvascular function in the ipsilateral side is strong, which indicates that the facial skin microvascular function is significantly impaired in the side with FNP compared to the healthy side via LSCI. Moreover, in some causes and phases of FNP, the remarkable difference between both sides of face was detected. Meanwhile, the improvement of ipsilateral perfusion and the narrowed gap between both sides' perfusion after treatments are observed. Therefore, we maintain that facial nerve diseases can cause the cutaneous microvascular dysfunction at the ipsilateral side of the face leading to the sensory dysfunctions of numbness and tightness at the affected side. Furthermore, the dysfunction is reversible based on the LSCI results. Nevertheless, the specific change and mechanism underlying the microvascular dysfunction are not sure.

Microcirculation is the blood circulation in the smallest scale of blood vessels, which is less than 100 µm in diameter, namely capillaries, arterioles, and venules. The microvessels on the arterial of the microcirculation are well-innervated and surrounded by smooth muscle cell which regulates the blood flow through metabolic, myogenic, and humoral control. Microcirculation consists of two important plexuses, the upper plexus and the lower plexus [6]. The lower plexus supplies lateral tributaries supports the hair bulbs and sweat glands, while the upper plexus serves as a thermal radiator. The main functions of the microcirculation are the supply of oxygen and nutrients and the removal of carbon dioxide. Moreover, the skin equips a high density of nerve fibers compared to other tissues, which indicates the major role of neural control on skin microvascular function [7].

Mechanisms of the microvascular regulation are complicated, which involves both neurogenic and humeral control [8–10]. The vasoconstriction and vasodilation of cutaneous circulation are controlled under neurovascular mechanisms. The vasoconstrictor regulation of the skin circulation is via adrenergic nerve. On the contrary, the vasodilation has a non-adrenergic mechanism. To sum up, the activities of cutaneous circulation based on the peripheral nerves are generating sweat and temperature regulation [11]. According to the facial anatomy and clinical features, we infer some nerves which may have a relationship with facial microcirculation: facial nerve, trigeminal nerve, great auricular nerve and sympathetic parasympathetic nerve. The emergence of an intraneural edema is likely to be the main factor in the pathophysiological process of FNP in recent years [12]. Since facial nerve lesion could lead to its branches and peripheries dysfunction, we infer that the latter one may generate the local microvascular disorder. However, the explicit reason and the role of microvascular dysfunction in the progress of FNP need further study.

In our department, LSCI is a requested examination for every FNP patient during the first visit. Regarding the medication management, we prefer drugs that improve the microcirculation. During a 6-month treatment, the increase in perfusion at different speeds can be noted. After an average of 6 months of treatment, we notice that the perfusion of the affected side of the face excels the contralateral one. According to this observation, we assume that it is the adequate medication management that leads to an excessive microvascular perfusion in ipsilateral side. Therefore, we regard the excess as a symbol of quitting the medication management and give patients only physical treatment.

Melkersson–Rosenthal syndrome is a rare neurological disease typified by recurring facial paralysis, relapsing orofacial edema and occurring of folds and furrows in tongue. The cause and pathogenesis of Melkersson–Rosenthal syndrome are unknown. The reason why there is a weak correspondence between the ipsilateral side and the contralateral side would be due to the recurring paralysis on both sides. Clinical proofs have shown that patients with Melkersson–Rosenthal syndrome tend to have recurrent FNPs occurring on both sides of face [13]. Thus, our study focuses on the perfusion results of bilateral recurrent FNPs, which shows that there is no significant difference between both sides of the face. Therefore, it is suggested that the bilateral FNPs can lead to bilateral microvascular malfunction according to the approximate bilateral perfusion results. On the contrary, during the recurrent history, compensation could take place on both sides of face, which could also lead to similar results.

In addition, there are also some subjects whose LSCI results do not show any significant difference. We maintain that the left–right asymmetry of the facial microcirculation would be a factor causing the phenomenon [14].

Nevertheless, limitations have been detected during the study. First, another study has showed the depth of skin microvessels is deeper than the penetration depth of LSCI (300 mm) for 1–1.5 mm [15]. Therefore, inaccuracy would be noticed. Second, during the study, we found lesions on the skin, such as acnes and acupuncture marks, can show a high microvascular perfusion, which may be due to their microvascular impact. Hence, errors would occur if skin lesions appear near the ipsilateral eyelids.

It is obvious that the compression and injury of facial nerve can generate long-term denervated degenerated muscles which subsequently result in the motionlessness at the ipsilateral side of the face. Together with the motionlessness, the stiffness, numbness and tightness should be taken into concern as well.

In FNP patients, difference of microvascular perfusion between the ipsilateral and contralateral side of the face can be observed from onset of the disease according to the result of the acute phase group. Moreover, the difference can change along with the treatment but would last after the treatment. Therefore, on one hand, LSCI can be used to measure the facial microvascular perfusion. In the meantime, LSCI can be a practical application in FNP patients. On the other hand, the application of LSCI reveals the microvascular dysfunction in the ipsilateral side of FNP patients compared to the contralateral side.

Conclusion

In spite of limitations, we trust the details provided in this research have advantages which can help clinicians decide the most appropriate therapeutic strategy for their patients.

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