

**The Clinical Report of the Therapy Result by Using
SLT Semiconductor Laser Therapy Instrument Nasal
Cavity Inner-Irradiation Through Single Photon
Emission Computed Tomography**

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The Single-use Light Transmission Nasal Cavity Plug and SLT Semiconductor Laser Therapy Instrument manufactured by Zhongqiang Medical Instrument Ltd., Shunde, Guangdong was the project (No.2KMO1001C) highly recommended by the Department of Science and Technology, Guangdong Province. The safe test had already been done by the Fundamental Medical Institute of Chinese Academy of Medical Science, and it had already been registered in the National Food and Drug Administration (No. 2000-3240067). It has been authorized to be produced by Guangdong Drug Administration (No.20010360). According to the suggestions of Guangdong Drug Administration on June 19th 2002, Clinical trial must be performed before volume-production and launch. Peking University Shenzhen Hospital was authorized as the hospital for the clinical trial, to visualize its curative effects with Single Photon Emission Computed Tomography (SPECT) for 2 months.

I. BACKGROUND

Laser is one of the greatest inventions of human being in the 20th century and it has been widely applied in all kinds of aspects. In 1990, Professor Wang Tiedan introduced the Low Energy Laser Irradiation Therapy from the pre-USSR, which immediately stimulated an upsurge of research and usage in our nation. The clinical application of laser was the representative case of combinations between modern high-tech and medicine.

The earliest Low Energy Irradiation Therapy was to use He-Ne laser inner-vascular irradiation. The fact that it must be pierced into the blood vessels suggested that it could only be used for a limited time; furthermore, inner-vascular infection and trauma might be induced. Therefore, in 1998, Zhongqiang Medical Instrument Ltd., Shunde, Guangdong commenced the development program of Single-use Light Transmission Nasal Cavity Plug and SLT Semiconductor Laser Therapy Apparatus. The therapy method had been improved and the risks caused by perforation reduced.

The clinical value of low energy irradiation therapy had already been approved. Searching through Literature implied that it had mainly been applied on cerebral disease, cardiovascular disease, diabetes etc. with good results obtained. Many researchers intended to understand the principle of low energy irradiation, they investigated from many aspects such as photics, bio-physics, anatomy, physiology, biochemistry, immunology, nuclear medicine, imaging and molecular-biology, but still could not make it clear. Currently there are 3 theories which have been widely accepted: (1) energy released from laser is a type of stimulation. These stimulations act on local tissue and/or multi-sensors on the vascular wall and excite them, including neuromuscular spindle, free nerve ending,

Pacini's corpuscles, Krause end bulb, receptor of follicul etc. The sensors which receive laser stimulation and the introduction structures are mainly probably the dissociate nerve twigs beside the micro-artery. Once the stimulation signals enter the brain and are conformed there, they are distributed to relevant brain sections to facilitate the synthesis of encephalic nerve nucleic acid and the replication of DNA, as well as adjusting the functions of enzymes, enhancing brain blood perfusion, stimulating the functions of encephalic-nerve cells, replacing, nourishing, repairing and regenerating scathed cells and eliminating pathological processes. (2) through the transduction and release of laser energy, nerve-internal secretion system, including insulin, sex hormone (testosterone, estradiol, prolan B luteinizing hormone, follicle-stimulating hormone), PRL, SOD, thyroid hormone, T lymphocyte group, immunoglobulin and alexin etc. can be regulated. This regulation has the characteristics of integrativeness and double-tropism. (3) Chinese traditional medicine believes that the head is the aggregation of all kinds of "Yang". "Du Mai" is the sea of "Yang Mai", "Ren Mai" is the sea of "Yin Mai", "Du Mai" and "Ren Mai" meets in the face. Nose situates on the exact centre of the head and it has "Du Mai", "Shou Zu Yang Ming Jing" and "Zu Tai Yang Jing" passing though. Therefore, laser stimulation in the nose could open "Jing Luo" (the nerve network), accelerate the circulation of blood and "Qi" (stamina) and hence can be the cure for many disorders.

II CLINICAL TRAIL DESIGN

1. Object

(1) Migraine (in general paroxysm period) 23 cases, while 11 occur

in the left brain, 8 in the right brain and 4 in both. 12 patients were male and 11 were female, their ages were between 15 ~ 70 years with an average of 45 ± 18 years; the courses of their diseases were 0.5 ~ 51 years. There were no positive physical sign during nerve system examination and the same results obtained by CT and MRI. No patient had taken cardiovascular or relational medication within 1 month.

(2) 10 cases of cerebral block, accordant to the Diagnosis Standard^[1] established by the 4th National Cerebral Vascular Conference in April, 1996. Among all patients, 4 were male and 6 were female, their ages were between 48 ~ 80 years with an average of 69 ± 10 years. The courses of their diseases were 2 ~ 12 months, which were confirmed by CT or MRI. There were 4 cases in the right basal ganglion, while 3 in the left and 3 with multiple cerebral infarction.

2. Method

(1) SPECT imaging. SPECT brain perfusion imaging was applied before and during the low energy inner nasal cavity irradiation to observe the temporal effect of the improvement on the brain blood perfusion and function.

(2) Low energy inner nasal cavity irradiation, using SLT semiconductor laser therapy apparatus manufactured by Zhongqiang Medical Instrument Ltd., Shunde, Guangdong, power 3.0mW , wavelength 650nm. Either left or right nasal cavity was randomly selected and the single-use laser transmission plug was inserted. The first SPECT brain perfusion image was taken before irradiating, the irradiation proceeded for

30 minutes while the original body position was kept, the second SPECT image was then taken.

(3) Brain perfusion imaging and imaging equipment, tracer ^{99m}Tc -ECD, offered by China Atomic Institute of Technology. The equipment was SIEMENS DIACAM /E.CAM/ ICON SPECT, with the low energy all-purpose collimator, rotating radius 13.5cm.

(4) Qualifications of image gathering and data operation referred to the Diagnosis And Therapy Criteria Of Nuclear Medicine^[2] by the Ministry of Health of People's Republic of China. The data gathering matrix was 128×128 , 360° rotation, 64 frames projection image, 5.6° /frame, collection time 15s/frame, Zoom=1.73 ,energy window width 20% (peak level 140keV). Image reconstruction: First, Butterworth low through filter function was applied to data process, cut-off frequency parameter $f_c=0.35$, gradient factor $n=12$; second, Ramp reverse projection was applied to reconstruct images and the attenuation correction was carried out by Chang method, the absorption coefficient $\mu=0.12\text{cm}^{-1}$, layer thickness was 5.4mm (2pixel).

All the conditions and the parameters of the two operations were the same. Due to the requirement of comparison analysis, the starting point and the end point of the layer image must be kept the same, as well as carrying out unitary process to make the two image data comparable.

(5) Images assembling display. For more convenient comparisons, the images were magnified onto the same screen according to the serial numbers of the same layer.

(6) Quantative process. Blood flow-function changing rate ,BFCR% mathematical model^[3] was applied. This model uses unitary method to calculate accurately the comparison result before and during the low energy irradiations. Since the brain blood perfusion and function state are relatively stable, commonly changes in local areas of the brain would not affect the whole brain significantly. Consequently, there exists a proportional relationship between certain local areas of the brain and the whole brain. Before the low energy inner nasal cavity irradiation, the relationship between local / whole brain is

$$L_b = C_b / \sum_{i=1}^{20} W_{bi}$$

L_b is the ratio of local / whole brain before the low energy inner nasal cavity irradiation; C_b is the local brain count before the irradiation (during the actual calculation, the average of the local brain counts of 2 ~ 3 layers would be taken); W_b is the whole brain count before the irradiation, which is the sum of the counts of 20 layers. The relationship between local and whole brain during the low energy laser inner nasal cavity irradiation is:

$$L_d = C_d / \sum_{i=1}^{20} d_i$$

L_d is the ratio of local / whole brain during the low energy inner nasal cavity irradiation; C_d is the local brain count during the irradiation; W_d is the whole brain count during the irradiation, which is the sum of the counts of 20 layers. BFCR% is :

$$C_d / \sum_{i=1}^{20} W_{di} - C_b / \sum_{i=1}^{20} W_{bi}$$

$$\text{BFCR}\% = \frac{\sum_{i=1}^{20} Cb / \sum_{i=1}^{20} Wbi}{Lb} \cdot 100$$

$$= (Ld - Lb) / Lb \cdot 100$$

The natural change of the whole brain BFCR% was 99%, with reliable range $t_{0.01} = 2.626$, 0.12 ~ 1.98%^[4]. In order to assure the reliability of the data, BFCR would be considered to be valid when set to be greater than 10%.

(7) Statistical process; Self-contrast; the differences between the local brain and the mirror opposite brain before and during the low energy inner nasal cavity irradiation were processed statistically using pairing “t” test.

3. Result

(1) Visual analysis. Before the irradiation, SPECT images of 23 cases showed that in each case there was one or two sections in the brain with low blood perfusion and functioning. The sections had various areas, most

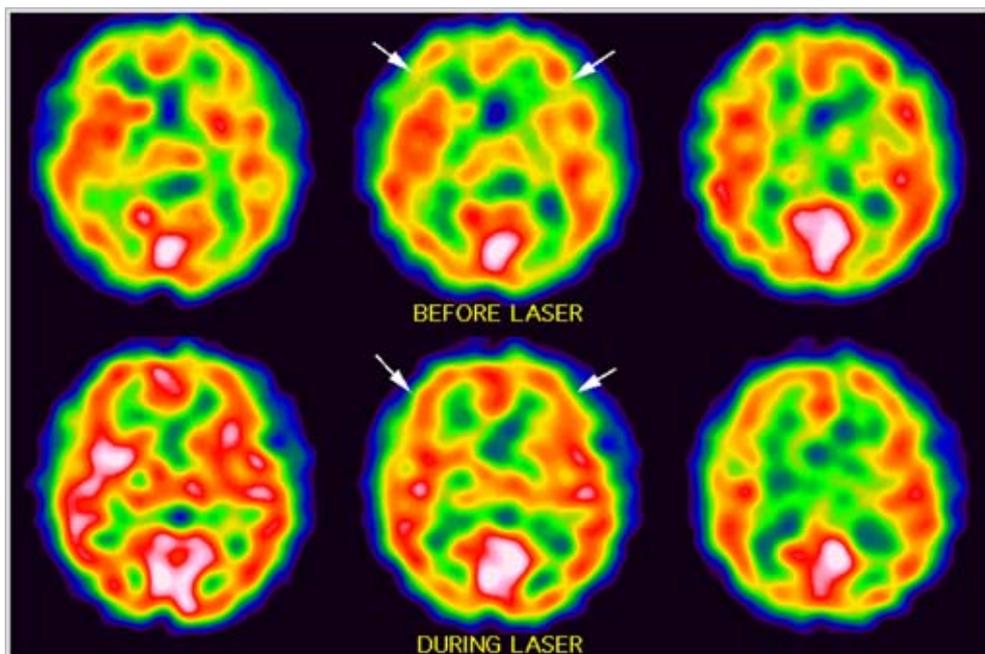


Fig. 1, the transversal image of the hemi crania patients. Before the laser inner nasal cavity irradiation SPECT showed that both temporal local blood perfusion and functioning were low (regions shown by arrows in the top row). After the 30-min-irradiation, the focuses shrank to different extent and/or disappeared (regions shown by arrows in the bottom row).

of them were of abnormal shape whereas only a few were approximately circular; a majority of the focuses were within the range of 1.5×2×2cm and the total number of focuses were 35. 11 patients whose headache were in the left had focuses in the left tempora, accompanied with 2 focuses in the Rolandic area, 1 in the forehead and 1 in optical lobe. Among the 8 patients whose headache were in the right, 7 had focuses in the right tempora, 1 in both temporas, all accompanied with 2 focuses in the forehead and 1 in optical lobe. 4 patients with double side headache had focuses in both temporas. When treated with low energy inner nasal cavity irradiation for 30 minutes, all focuses shrank to various extent and/or totally disappeared (Fig 1,2) . After the treatment, all the patients' headache symptoms alleviated or disappeared.

Before the laser inner nasal cavity irradiation, SPECT images of the 10 patients with brain block showed that there were 16 focuses with definite low blood perfusion and functioning in different parts of the brain, the result was matched by CT or MRI; however, the focuses were of slightly bigger size. After the irradiating for 30 min, the region with low blood perfusion and functioning caused by infarction shrank or/and disappeared,

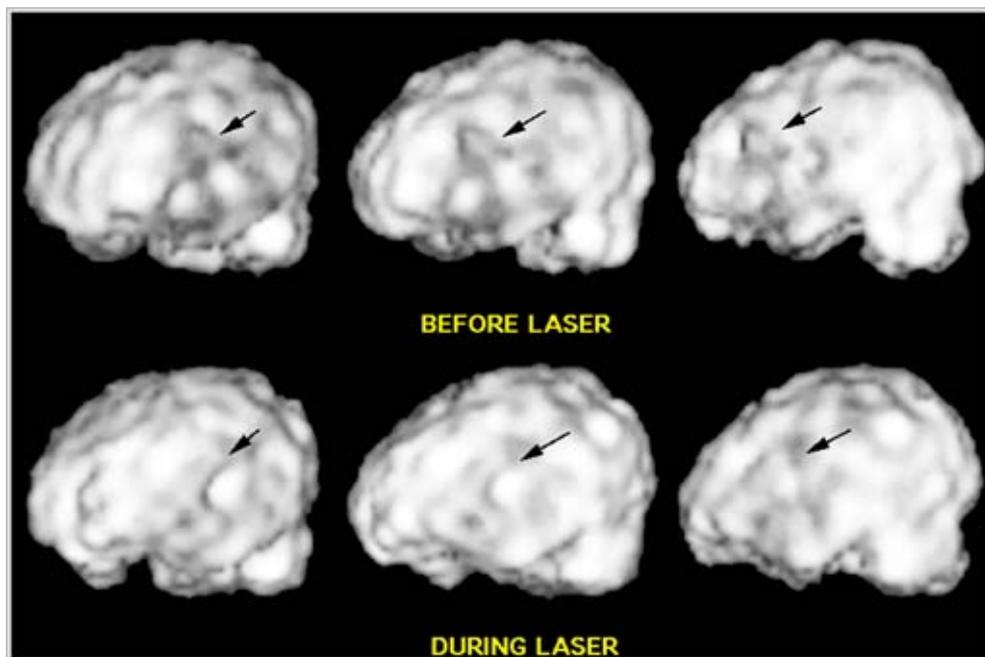


Fig. 2 a 3-dimensional image of the same patient in picture 1. Before the laser inner nasal cavity irradiation SPECT showed that both temporal local blood perfusion and function were low (regions shown by arrows in the top row). After the 30-min-irradiation, the focuses shrank to different extent

the clinical symptoms alleviated to different extent. Furthermore, there were various degree of recovery in the brain-opposite cerebellum mal-connection.

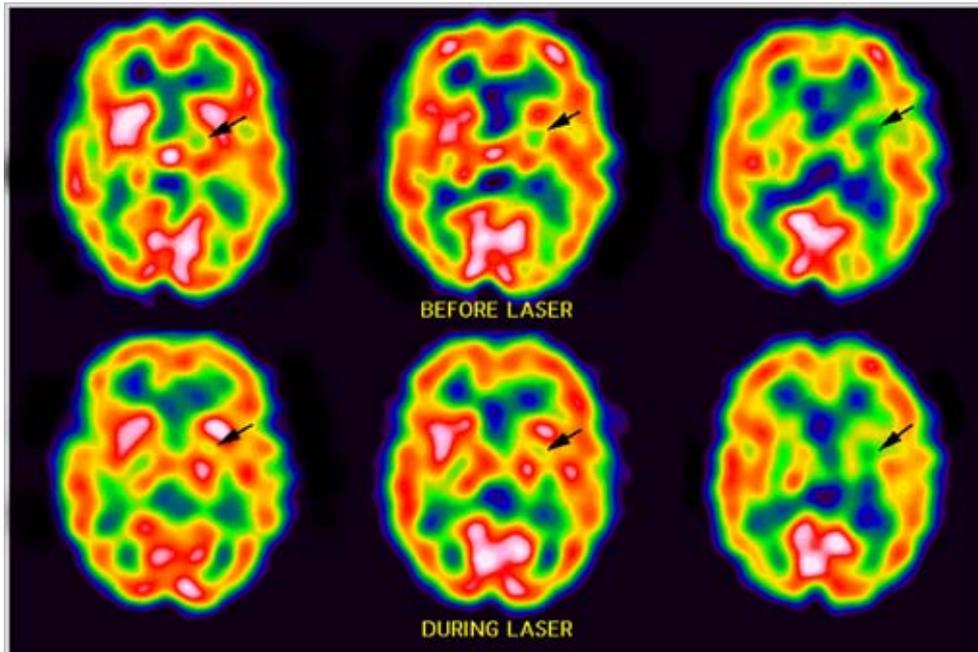


Fig. 3 the transversal images of left basal ganglion infarction patients. Before laser inner nasal cavity irradiation SPECT showed that left basal ganglion's local blood perfusion and function were low (narrow). After the irradiation for 30 min, the focuses were shrink and/or disappear for different level.

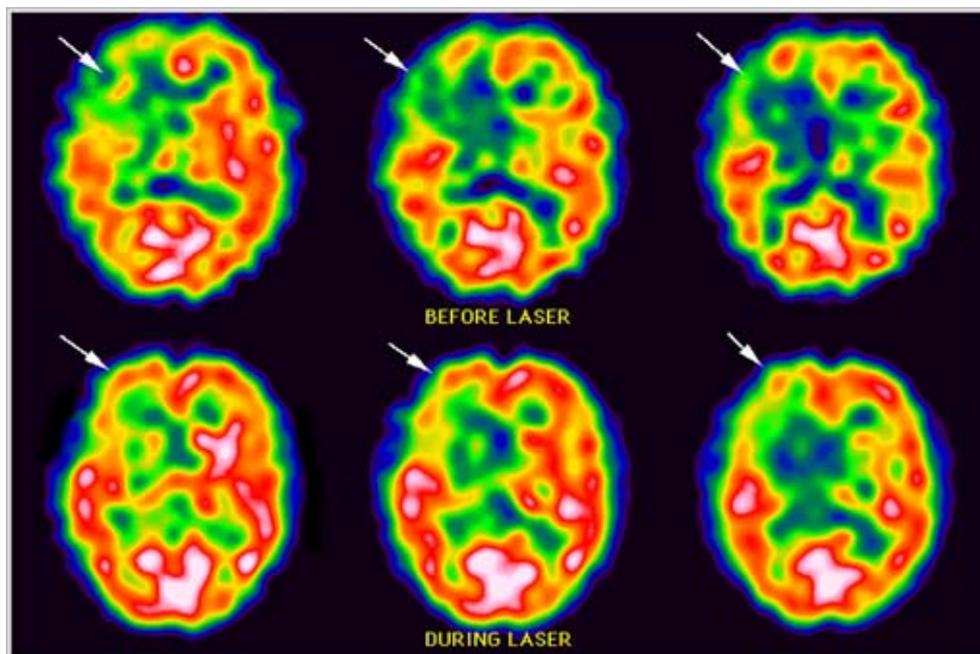


Fig. 4 the transversal image of multi-infarction patient. Before laser inner nasal cavity irradiation SPECT showed that right forehead's local blood perfusion and function were low (narrow). After the irradiation for 30 min, the focuses were shrink and/or disappear for different level.

(2) Quantitative analysis. Quantitative analysis was applied to 35 focuses and their mirror opposite focuses of the 23 patients. Before the laser irradiation, the differences between values of the focus Lb and the mirror opposite focus Lb were remarkable ($t=3.21, P<0.001$) ; during the 30-min-irradiation, the focus Ld was significantly higher than the pre-treatment focus Lb ($t=3.63, P<0.001$) , the mirror opposite Ld value was also higher than that of the pre-treatment Lb; nevertheless, there was no statistical differences ($t=0.95, P>0.05$)(Table 1). The BFCR% of the focuses were much higher than that of the mirror focuses, with notable differences ($t=2.89, P<0.001$). The BFCR% of the 32/35 focuses during the irradiation were larger than 10%, with efficiency ratio 91.43% (Table 2).

Table 1. the focuses and their mirror-opposite focuses of the 23 hemi crania patients before and after treatment and the BFCR% values (focus 35)

Position	Before Las. (Lb)	During Las. (Ld)	t	P	BFCR%
	$\bar{x}\pm s$	$\bar{x}\pm s$			$\bar{x}\pm s$
Focuses	9.42±2.70	11.85±2.90	3.63	<0.001	34.23±38.74
Mirro opp.	11.68±3.18	12.32±2.67	0.95	>0.05	11.67±25.26
t	3.21	0.71			2.89
p	< 0.001	> 0.05			< 0.01

Table 2 The degree of variation in BFCR% for the focuses of the 23 patients (35 focuses)

	degree of variation in BFCR%			
	(±)	(+)	(++)	(+++)
Focuses	3	12	8	12
Percentage (%)	8.57	34.29	22.86	34.28

①±: brain blood perfusion and functioning enhanced slightly, $10\% > \text{BFCR}\%$;

②+: brain blood perfusion and functioning enhanced, $10\% \leq \text{BFCR}\% < 20\%$;

③++: brain blood perfusion and functioning enhanced markedly, $20\% \leq \text{BFCR}\% < 30\%$;

④+++ : brain blood perfusion and functioning enhanced extraordinarily, $30\% \leq \text{BFCR}\%$

Quantitative analysis was applied to 16 focuses and their mirror opposite focuses of 10 patients (chart 3). Before the laser irradiation, the values of the focuses Lb were distinct from that of their mirror opposite focuses ($t=4.80, P<0.001$); while during the 30-min-irradiation, the focus Ld was much higher than the pre-treatment focus Lb ($t=3.49, P<0.001$), the mirror opposite Ld was also higher than that of the pre-treatment mirror opposite Lb; however, there were no statistical differences ($t=0.53, P>0.05$) (Table 1). BFCR% of the focuses was much higher than that of the mirror focus, with notable differences ($t=4.28, P<0.001$). BFCR% of the 14/16 focuses during the irradiation was greater than 10%, with efficiency ratio was (chart 4).

Table 3 focuses and their mirror-opposite focuses of 10 hemi crania patients and the BFCR% values (focus 16)

Position	Before las. (Lb)	During Las. (Ld)	t	P	BFCR%
	$\bar{x} \pm s$	$\bar{x} \pm s$			$\bar{x} \pm s$
Focuses	9.37±1.84	11.765±2.30	3.49	< 0.001	12.57±1.74
Mirro-opp.	12.27±1.68	12.59±1.74	0.53	> 0.05	2.64±8.02
t	4.80	1.18			4.28
p	< 0.001	> 0.05			< 0.001

Table 4 The degree of variation in BFCR% for the focuses of the 10 patients (16 focuses)

	The degree of variation in BFCR%			
	(±)	(+)	(++)	(+++)
Focuses	2	5	5	4
Percentage (%)	12.5	31.25	31.25	25

- ①±: brain blood perfusion and function enhanced slightly, $10\% > \text{BF CR}\%$;
- ②+: brain blood perfusion and function enhanced, $10\% \leq \text{BF CR}\% < 20\%$;
- ③++: brain blood perfusion and function enhanced markedly, $20\% \leq \text{BF CR}\% < 30\%$;
- ④+++: brain blood perfusion and function greatly extraordinarily, $30\% \leq \text{BF CR}\%$

4. Conclusion

(1).SPECT technique possesses special value: ① visualization of the treatment by the low energy inner nasal cavity irradiation. SPECT could directly visualize the brain blood perfusion and functioning during the low energy inner nasal cavity irradiation. ② It does no damage to human body (alive) during the research. Since the whole laser experiment has been completed on human body under real physiological and pathological circumstances, it is an improvement comparing to experiments on animals. ③ quantification of data of the low energy laser irradiation images. The utilization of software to read the data as well as BF CR% mathematical model and physiological mathematical model to quantify the huge data of the low energy laser irradiation images, objectively evaluated the clinical value of SLT semiconductor laser therapy apparatus on treating cerebral diseases.

(2) The value of SLT semiconductor laser therapy apparatus on the hemi crania has been confirmed. During the 30-min-irradiation, the focus Ld became significantly higher than the pre-treatment focus Lb ($t=3.63, P<0.001$) , BF CR% of the mirror opposite Ld also grew higher than that of the pre-treatment value, with notable difference ($t=2.89, P<0.001$) . BF CR% of the 32/35 focuses during the irradiation was large

than 10%, accompanied with alleviation in headache symptom; the efficiency ratio was 91.43%. The result showed that the low energy inner nasal cavity irradiation treatment could ameliorate the corresponding blood perfusion in the focuses of migraine patients, enhance brain functioning and alleviate headache symptoms.

(3) The value of treating cerebral block using SLT semiconductor laser therapy apparatus has been confirmed. During the 30-min-irradiation, focus Ld values of the 10 patients became much higher than that of the pre-treatment focus Lb ($t=3.49$, $P<0.001$). BFCR% of the focuses were also much higher than that of the mirror focus, with significant differences ($t=4.28$, $P<0.001$). BFCR% of the 14/16 focuses during the irradiation were larger than 10%, the efficiency ratio was 87.5%. The result showed that the low energy inner nasal cavity irradiation could improve the local blood perfusion and brain cell functioning, ameliorate the deficiency in oxygen, stimulate the activities and metabolism in cerebral cells and accelerate the rehabilitation of injured nerve cells. At the same time, it could be regard as one of the indexes to evaluate the extent of injury of cerebral cells.

(4)The worthiness of promoting the utilization of SLT semiconductor laser therapy apparatus: ① No trauma. During the treatment, the laser equipment would be placed in the physiological channel - nasal cavity, which can easily be accepted by the patients. ②Single-use. There had been no intercross infection during the experimental period of the single-use Light Transmission Nasal Cavity Plug. ③Portable. The laser

equipment is small enough to be used under many conditions. ④Simple and easy operation made it suitable for usage in both hospitals and families; ⑤ High-quality equipment. There had been no failure in functioning during the experimental period. ⑥Low cost in the treatment, which could be accepted by the majority of patients.

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