BLOOD FLOW IN THE LIMBS OF HEMIPLEGIC PATIENTS BY $^{99m}$Tc-HSA ACCUMULATION CURVE AND DIGITAL PLETHYSMOGRAPHY

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Abstract: A) Using $^{99m}$Tc-Human-Serum-Albumin (HSA) accumulation curve we have studied the blood flow in the lower extremities of the hemiplegic patients. After injection of 5-10 mCi of $^{99m}$Tc-HSA into v. mediana cubiti by the Oldendorf method, we recorded the RI count from both knees. We have examined 68 hemiplegic patients (male: 26, female: 42, right: 31, left: 37, average age: 61.7 years, average Brunnstrom stage of the lower extremity: 3.73, average duration post-stroke: 20.2 months). We counted the accumulation of the isotope in both knees 1 and 30 minutes after injection, and calculated the percentage (paretic side/right and left sides), and named them as "1-minute value" and "30-minute value".

RESULTS
1) During the 15 months period after an attack, the paretic leg had more blood flow than the non-paretic leg.
2) After 15 months after attack, on the contrary, the paretic leg had less blood flow than the non-paretic leg.
3) This tendency is clear in the left-sided hemiplegic patients.
4) There is no relation between the blood flow and age, and the Brunnstrom stage, and the ability to walk.

B) Using digital plethysmography, we have studied the blood flow in the finger and toe, too. We have examined 57 hemiplegic patients. We have averaged the five heights of the wave (mV/V), and calculated the percentage involved (paretic side/right and left) and labeled it "the paretic blood flow value (of the finger and of the toe)".

RESULTS
1) During the 12 month period after an attack, the paretic side had more blood flow than the non-parietic side.
2) After 15 month after an attack, on the contrary, the paretic side had less blood flow than the non-paretic side.
3) This tendency is clear in the finger than the toe.
4) There is no correlation between the blood flow and the age, and the Brunnstrom stage, and the ability to walk.

I) Purpose
In order to study the state of the circulation of the upper and lower extremities of the hemiplegic patient after a cerebral apoplexy attack, we have proceeded by accumulation curve using $^{99m}$Tc-Human Serum Albumin (HSA) of the lower extremities, and using the digital plethysmography at the upper and lower extremities.

A) Accumulation curve by $^{99m}$Tc-HSA

II) Technique
After injection of 5-10 mCi of $^{99m}$Tc-Human Serum Albumin (HSA) into V. mediana cubiti by the Oldendorf method\(^1\), we recorded the RI count in both knees, and took a photo of scintigram with GCA 102 and RGA 102 (made by Toshiba).

III) Test cases

Test cases were 68 cases of hemiplegic patients, right hemiplegy 31: left 37, men 26: women 42, age: 42-80 (average 61.7 years), duration from the attack 1-88 months (average 20.3 months), Brunnstrom stage of the leg I-VI (I: 3, II: 6, III: 15, IV: 23, V: 15, VI: 2, unknown: 4, average: 3.73). In order to provide a contrast, we applied the same study to seven cases of orthopaedic and non-hemiplegic patients.

IV) Hypothesis

In the former, identical study done by Maruyama\(^2\), in which he stated that "from identical examinations of the same patient many times after an attack, the paretic leg has more accumulation than the non-paretic leg within one year of the attack but after 1 year following an attack, the non-paretic leg has more accumulation than the paretic leg".

From these results, and from our new results on the study of accumulation, we made an hypothesis that the paretic leg has more accumulation than the non-paretic leg within 15 months of an attack, but 15 months after an attack, the non-paretic leg has more accumulation than the paretic leg.

The following is a statistical examination of this hypothesis.

V) Results

We counted the accumulation of isotopes in both knees 1 and 30 minutes after an injection, and calculated the percentage (paretic side/right and left sides), and denoted them as "1-minute value" and "30-minute value".

We made a chart placing these values on the vertical line and months after attack on the horizontal line.

1) 1-minute-value

We made a chart placing the 1-minute value on the vertical line and months after attack to the examining time on the horizontal line, and drew dotted lines at 50 %, which indicates equal accumulation in both knees, and 15 month, which indicates the turning period of our hypothesis (Fig. 1).

The number in the small circle is the Brunnstrom stage of the leg at the time of examination.

In this chart, we counted the cases which match our hypothesis, namely, cases over 50 % and under 14 months, or cases under 50 % and over 15 months.

Further, we counted the cases which do not fit our hypothesis, namely, the cases under 50 % and under 14 months, or the cases over 50 % and over 15 months.

We disregarded the cases on the dotted line. (50 % and 15 months: 13 cases).

The number of cases which fit and do not fit our hypothesis are 40 vs 15, thus the confirmation rate is 72.7 % (40/55).

2) 30-minute value

We made the same chart from the 30-minute value and months after attack.

On this chart, the cases of 50 % of accumulation decrease to only 4 cases from 13 cases on the 1-minute value chart.

The number of cases which fit and do not fit our hypothesis are 44 vs 20. The confirmation rate is 68.8 % (44/64) (Fig. 2).

3) 30-minute value of right hemiplegy

Considering these two charts, there are
few cases of equal (50%) blood flow in the 30-minute value, so we think the 30-minute value will better indicate the blood flow than the 1-minute value. Also, we did additional examinations with the 30-minute value.

In the 30-minute value of right hemiplegy chart, the confirmation rate of our hypothesis is 60.7% (17/28) (Fig. 3).

The cases connected on the line are the same patients examined after a few months.

We examined 6 patients again, and 4 cases indicate decrease in the right ward.

They indicate that in the first period after the attack, the paretic leg has more blood flow than the non-paretic leg, but after some months more, the paretic leg has less blood flow than the non-paretic leg (our hypothesis).

We indicated that phenomenon by the accumulation curve of the typical cases.

Case-A
Right hemiplegy by cerebral apoplexy, Brunnstrom stage (leg) II, the 54-year-old woman had more blood flow in the right knee (paretic leg) than the left in the 5 months after the attack chart, but in the 6 months after the attack chart, both knees have equal blood flow (Fig. 4).

After 45 months, the left knee (non-paretic leg) has more blood flow than the right.

4) 30-minute value of left hemiplegy
In the 30-minute value of left hemiplegy chart, the confirmation rate of our hypothesis is 72.2% (26/36) (Fig. 5).

We examined 8 patients again, and 5 cases indicate a decrease in the right ward.

Case-B
Left hemiplegy by cerebral apoplexy, Brunnstrom stage (leg) IV, the 68-year-old man...
had more blood flow in the left knee (paretic-leg) than the right 14 months after the attack.

But after 23 months, the right knee (non-paretic leg) had more blood flow than the left (Fig. 6).

In this same period, we took a multiform photography of this patient once every second after an injection.

This photo indicates that after only three seconds, the shape of the right femoralis artery is seen, and after 5 more seconds the shape of the left femoralis artery is seen but less clearly than the right (Fig. 7).

Considering these charts of left and right hemiplegy, we think that the left hemiplegy is closer to confirming our hypothesis than the right.

5) Blood flow in non-paretic patients

In order to provide a contrast to the hemiplegic patients, we performed the same study on non-paretic and orthopaedic injury cases (7 cases) (Fig. 8).

Fig. 6 Case-B (T. S.): left hemiplegy (by apoplexy), 68 y, man, Brunnstrom stage-IV, 99mTc-HSA accumulation curve

Fig. 7 Radionuclide Angiogram 99mTc-HSA (i. v.) both knees.

Fig. 8 Non-paretic disease.
(one-minute value)
(by 99mTc-HSA accumulation curve)
In order to match the ages of the hemiplegic patients, 5 cases are fractures of the neck (femur) and 2 cases are osteorathritis of the hip.

From this chat, we conclude that injured legs have less blood flow, in general.

VI) Discussion

1) Statistical discussion

a) Correlation between accumulation in the paretic leg and months after attack.

We did a statistical analysis on the correlation between accumulation in the paretic leg and the months elapsed after the attack.

(1) Simple correlation coefficient.

The simple correlation coefficient of these 68 cases is, 1-minute value: \(-0.254\), 30-minute value: \(-0.375\), so we only used the 30-minute value after that.

(2) Spearman's rank correlation coefficient.

The months elapsed after an attack to the examining time and accumulation are not related to the normal distribution of the population, so we tested using Spearman's rank correlation coefficient.

In the 30-minute value, the coefficient is: right hemiplegy: \(-0.458\), and left hemiplegy: \(-0.410\).

On Spearman's correlation table, the abandonment number is \(r_{30} = 0.306\) (n=30, significant level=0.05).

The absolute of the correlation coefficient of the right hemiplegy and the left is bigger than the abandonment number, so, the result of this test is that "there is some correlation between accumulation in the paretic leg and the months after the attack to the examining time".

And furthermore, "there is more correlations in the left hemiplegy than the right".

(3) The experimental formula (regression equation)

We made a experimental formula \((y = a - \frac{b}{x} + \frac{c}{x^2})\) and tested it by the method of least squares (Fig. 9).

The result of this test is that "accumulation in the paretic leg is greater than in the non-paretic leg within several months of an attack, but after that, on the contrary, the paretic leg has less accumulation".

The turning period of this experimental formula is from eight to thirty months, so we must examine further in order to determine the exact period.

b) Correlation between accumulation in the paretic leg and the Brunnstrom stage of the leg.

(1) Simple correlation coefficient.

The simple correlation coefficient between accumulation in the paretic leg and the Brunnstrom stage of the leg is \(r_s = 0.0807\).

(2) Spearman's rank correlation coefficient.

The coefficient is \(r_{s2} = 0.012\).

The absolute value of this coefficient is smaller than the abandonment number (\(r_{30} = 0.306\)), so the result of this test is that "there is no correlation between accumulation in the paretic leg and the Brunnstrom Stage" (Fig. 10).

c) Correlation between accumulation in the paretic leg and the ability to walk.

(1) Simple correlation coefficient.

We tested the correlation between accumulation in the paretic leg and the ability to walk.

We divided the ability to walk into ① inability to walk, ② ability to walk with support, ③ ability to walk without support. The simple correlation coefficient is \(r_w = 0.264\).

(2) Spearman's rank correlation coefficient.

The coefficient is \(r_{w2} = -0.036\).

Fig. 9 Experimental formula: \(y = a - \frac{b}{x} + \frac{c}{x^2}\) (by \(^{99m}\)Tc-HSA accumulation curve)
Fig. 10 Correlation between the accumulation of the paretic leg and Brunnstrom stage (by 99mTc-HSA accumulation curve)

Fig. 11 Correlation between the accumulation of the paretic leg and the ability to walk (by 99mTc-HSA accumulation curve)

The absolute value of this coefficient is smaller than the abandonment number ($r_{30}=0.306$), so the result of this test is that "there is no correlation between accumulation in the paretic leg and the ability to walk" (Fig. 11).

d) Correlation between accumulation in the paretic leg and the age

(1) Simple correlation coefficient.

We tested the correlation between accumulation in the paretic leg and age (Fig. 12).

The simple correlation coefficient is $r_a=0.333$.

(2) Spearman's rank correlation coefficient.

The coefficient is $r_{a2}=0.038$.

The absolute value of this coefficient is smaller than the abandonment number ($r_{30}=0.306$), so, the result of this test is that "there is no correlation between accumulation in the paretic leg and age".

2) Blood flow scanning using RI

a) Scanning of the blood vessel

There are many measurement methods of digital blood flow\(^3\), such as plethysmography, arteriography, venography, lymphoangiography, venous pressure, radioisotope, etc, but it is very difficult to decide the best and the most effective method to use, because the blood flow of the every organ and tissue is different, including flow in the limbs such as in bone, muscle, skin, etc. The controlling nerve systems of the blood vessels involved are different and complicated (Fig. 13).

Furthermore, the controlling system is different when the subject is at rest or exercising.

Since the blood flow to every tissue is not equal to the volume of the feeding artery, it is not easy to choose one method and understand the results of that method.

There are two ways using radioisotopes.

The first method is perfusion scanning, using radioisotopes and a particle, such as albumin, and injectioning it into the artery.

The second is clearance scanning, using radioisotopes directly into the tissues. The first method is effective for studying whole circulation through the blood vessels, and the second method is effective for studying blood flow to the one or some tissues, including the capillaries. However, in the
Fig. 12 Correlation between the accumulation of the paretic leg and the age.
(by $^{99m}$Tc-HSA accumulation curve)

Fig. 13 Method of the measurement of the digital blood flow

1. Plethysmography
2. Arteriography
3. Venography
4. Lymphangiography
5. Venous pressure
6. Intraosseous pressure
7. Ergography
8. Radiosotopes
9. Heated thermocouple method
10. Skin thermometry
11. Muscle thermometry
12. Sweating
13. Capillary nailbed microscopy
14. Infrared photography
15. Oscillometry
16. Calorimetry

first method, it is difficult to differentiate the circulation to every tissue, such as bone, muscle or skin, and in the second, it is difficult to study whole circulation in the human body.

b) The meaning of our blood flow study by $^{99m}$Tc-HSA

We think that the one-minute value indicates the blood flow of the arterial phase and the 30-minute value indicates the blood flow of all vessels (arteries, veins and capillaries) of the leg by our accumulation curve.

The $^{99m}$Tc-HSA, which was injected from the V. mediana cubiti, circulated through the body, and “some of it diffused from the vessels but almost of it remained in the vessels for some hours” (by Herbert).

As seen in the scinti photo at every second after injection, both figures (lines) of the femoralis artery are seen after few seconds, and at this time, the difference of the right and left can be clearly recognized.

The difference continues for 30–60 seconds, and during these seconds, the figures of the femoralis artery are clearly recognized.

We think, therefore, that accumulation after 60 seconds indicates the accumulation of the artery, namely, the blood flow of the artery.

Accumulation in the leg will reach a plateau after 15 to 30 minutes and remain in this condition for over 2 hours.

We think of this condition (the plateau) as “the condition of a balance between inflow from the artery and outflow from the vein (by Takaya in 1980)”.

We thus choose 30-minute value as the indicator of this plateau and this value indicates “the blood flow in the leg (artery, vein and capillary)”.

In some cases, we examined digital plethysmogram, and we obtained the same difference and results from that, so we think this accumulation curve by $^{99m}$Tc-HSA indicates “blood flow”.

B) Digital plethysmography

II) Technique

After 30 minutes' rest, the transducer was applied to the middle finger and big toe, and digital plethysmography was recorded by PT-300 (made by Fukuda).

Thus, we have averaged the five heights of the wave (mv/v), and calculated the percentage involved (paretic side/right and left), and labeled it “the paretic blood flow value (of the finger and of the toe)”. 

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III) Test cases.
Test cases were 57 cases of hemiplegic patients, right hemiplegy 22: left 35, men 38: women 19, age: 45-81 (average 64.6) years, duration from the attack to the examining time: 1-156 (average 17.1) months, Brunnstrom stage average: arm 4.4, leg 5.3.
These patients are not the same patients who underwent accumulation curve study.
IV) Results
We made charts placing “the paretic blood flow value” onto a vertical line, and the months after attack to the examining time onto a horizontal line (Fig. 14) (Fig. 15).
The number in the small circle is the
Brunstrom stage at the examining time, and the cases connected by the line are the same patients, examined after a few months.
From these charts, there are many cases which indicate “paretic blood flow value” over 50% until 12 months after an attack, namely, which have more blood flow in the paretic side than the non-paretic side.
However, after 12 month, there are many cases which indicate “paretic blood flow value” under 50%, namely, which have less blood flow in the paretic side than the non-paretic side.
These tendencies are clearer in the finger than in the toe.
Therefore, we tested these results statistically.
V) Statistical discussion
a) Correlation between paretic blood flow value and the month after an attack to the examining time.
(1) Spearman’s rank correlation coefficient.
The month after an attack to the examining time and paretic blood flow value are not related to a normal distribution of the population, so we tested using Spearman’s rank correlation coefficient.
The coefficient of the finger is r (finger-month) =0.3754, and the coefficient of the toe is r (toe-month) =0.0244.
The abandonment number from Spearman’s correlation table is r30=0.306 (n=30, significant level=0.05). Only the absolute number of that coefficient of the finger is larger than the abandonment number, so the result of this test is that
① There is some correlation between the “paretic blood flow value of the finger” and the months after an attack the examining time (Fig. 14).
② There is no correlation between the “paretic blood flow value of the toe” and the months (Fig. 15).
(2) For the experimental formula (regression equation).
We made a experimental formula (regression equation) (y=a−b/x+c/x^2) used in the accumulation curve test, and we tested by the method of least squares (Fig. 16).
Fig. 16 Experimental formula:
\[ y = 45.53 + \frac{20.42}{x} - \frac{7.07}{x^2} \]
(by plethysmography)

The result of this test was that the paretic blood flow value is larger than that of the non-paretic side within several months of the attack, but after that, on the contrary, the paretic blood flow value is smaller.

The turning period for this experimental

Fig. 17 Correlation between the blood flow of the paretic finger and the Brunnstrom stage (by plethysmography)

Fig. 18 Correlation between the blood flow of the paretic toe and the Brunnstrom stage.
(by plethysmography)

Fig. 19 Correlation between the blood flow of the paretic finger and the age (by plethysmography)
a) Correlation between paretic blood flow value and the age.

We tested with Spearman’s rank correlation coefficient. The coefficient of the finger is $r$ (finger-age) = 0.025, and that of the toe is $r$ (toe-age) = 0.078. (Fig. 19) (Fig. 20).

They are smaller than the abandonment number ($r_{30} = 0.306$), so the result of this test is that,

"There is no correlation between the paretic blood flow value (of the finger and toe) and the age."

c) Correlation between the paretic blood flow value and the ability to walk.

We divided the ability to walk into (1) inability to walk, (2) ability to walk with support, (3) ability to walk without support. We tested with Spearman’s rank correlation coefficient.

The coefficient is $r$ (toe-walking) = 0.051 (Fig. 21).

This coefficient is smaller than the abandonment number ($r_{30} = 0.306$), so the result of this test is that,

"There is no correlation between the paretic blood flow value of the toe and the ability to walk."

C) Discussion of literature

There are many studies and reports about blood flow in hemiplegy, but their methods and periods of examination are different, so their results are different (Fig. 22).
Fig. 22 Report of the blood flow of the hemiplegy

<table>
<thead>
<tr>
<th>author</th>
<th>year</th>
<th>method</th>
<th>result</th>
</tr>
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<tr>
<td>Weiss</td>
<td>1930</td>
<td>A-V O₂ difference</td>
<td>↑</td>
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<tr>
<td>Eliss</td>
<td>1936</td>
<td>A-V O₂ difference</td>
<td>arm ↑, leg ↑</td>
</tr>
<tr>
<td>Redish</td>
<td>1957</td>
<td>plethysmography</td>
<td>↑</td>
</tr>
<tr>
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<td>1962</td>
<td>plethysmography</td>
<td>↓</td>
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<td>1968</td>
<td>plethysmography</td>
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<td>Goldberg</td>
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<td>plethysmography</td>
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<td>Mizushima</td>
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<td>PSP</td>
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<tr>
<td>Kato</td>
<td>1975</td>
<td>Doppler</td>
<td>↓</td>
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<tr>
<td>Mashima</td>
<td>1975</td>
<td>³⁵⁹Xe wash out</td>
<td></td>
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<td>Kuriyama (1)</td>
<td>1981</td>
<td>⁹⁹⁹Tc-HSA</td>
<td>under 15 months ↑</td>
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<td></td>
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<td>over 15 months ↓</td>
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<tr>
<td>Kuriyama (2)</td>
<td>1983</td>
<td>plethysmography</td>
<td>under 12 months ↑</td>
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<td></td>
<td></td>
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<td>over 12 months ↓</td>
</tr>
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Only Mashima¹⁵ (1976) and we examined periodically after an attack; he used wash out ability of ¹³³Xe from muscle.

He stated that the blood flow in the muscle of the paretic's upper extremities is lower than that of non-paretic people, and he examined them periodically after an attack, indicating that the blood flow of the paretic side does not change, but that of the non-paretic side increases gradually⁴.

D) The blood flow of hemiplegic patients

We examined the blood flow of hemiplegic patients using two methods periodically after an attack.

From these two studies, we get the same results, namely, "the blood flow of the paretic side is greater than that of the non-paretic side for some months after an attack, but after that, the paretic side has less blood flow than the non-paretic side".

The turning period is about one year, according to the chart, but 8 to 30 months from RI study and 4 months from plethysmography, according to the statistical study. The reason for the difference in blood flow between the paretic side and the non-paretic side is unknown, but the blood flow of the paretic side is increased because of palsy of the capillary and the sympathetic nerves. (by Ellis⁷ in 1936 and Ueda¹⁴ in 1974).

However, the reason that the blood flow changes after one year is unknown.

We think this reason is due to the fact that:

1) The amount of exercise on the paretic side is small. A large blood flow is not required.

Gradually, as a response to life itself, the vessels become narrower, so blood flow in the paratic side decreases.

2) By the atrophy of the paretic muscles, so the blood flow in the paretic side decreases relatively.

E) Relationship between clinical symptoms and assay results

Complications of hemiplegia by circulatory disturbances, especially by blood congestion are often experienced in clinical practice.

The shoulder hand syndrome usually has chief complaints of swelling of the back of hand and pain of shoulder on the affected site. Ellis⁶,⁷ and Ueda et al.¹⁴ reported that the shoulder hand syndrome is largely developed within 5 months after onset of hemiplegia.
Maruyama\textsuperscript{21} and Hanakago et al.\textsuperscript{17} reported that heterotopic ossification tends to be developed on the paralyzed side within 1 year after the onset of paralysis.

Both of the above two diseases are ascribed to the circulatory insufficiency of the limbs on the affected side, i.e. blood congestion of the affected side. Ellis\textsuperscript{6,7}, Ueda\textsuperscript{14} and Takats et al.\textsuperscript{18} claimed the above etiology for the shoulder hand syndrome, while Nakajyo\textsuperscript{19} and Nakaseko et al.\textsuperscript{20} alike claimed the same etiology for heterotopic ossification. The clear-cut etiologies of these complications have not yet been clarified, but the fact identified by our two kinds of testing methods that the blood stream is of a larger volume on the paralyzed side within one year after onset of the paralysis indicates that the affected side is in the state of blood congestion at the early stage after the onset of hemiplegia, although the comparison of blood volume is made simply on a relative basis and may be interpreted as showing that the blood congestion on the affected side may act as the cause for various complications to hemiplegia.

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References