

2. Maddox J, Randi J, Stewart WW. "High-dilution" experiments: a delusion. *Nature* 1988; 334:287-290.
3. Benveniste J. Dr. Jacques Benveniste replies. *Nature* 1988;337:291.
4. McCutcheon CW. Peer review: treacherous servant, disastrous master. *Technology Rev* 1991;94:29-40.
5. Eisenberg D. *Encounters with Qi*. New York: Norton; 1985.
6. Sheikh AA, Sheikh KS. *Eastern and western approaches to healing*. New York: Wiley; 1989.
7. Chopra D. *Perfect Health*. New York: Crown; 1990.
8. Donden Y. *Health through balance*. Ithica: Snow Lion; 1986.
9. Porkert M, Ullmann C. *Chinese medicine*. Translated by Mark Howson. New York: William Morrow; 1988.
10. Wallace RK, Benson H. The physiology of meditation. *Sci Am* 1972;226:84-90.
11. International Symposium on Chinese Qigong Health Preservation and Qigong Techniques. Beijing: Foreign Languages Press; 1991.
12. Eliade M. *Yoga: immortality and freedom*. Translated by Willard R. Trask, Princeton: Princeton University Press; 1969.
13. Iyengar BKS. *The concise light on yoga*. London: Unwin; 1980.
14. Kovacs FM, Gotzens V, Garcia A, et al. Experimental study on radioactive pathways of hypodermically injected technetium-99m. *J Nucl Med* 1992;33:403-407.

EDITORIAL

Nuclear Medicine and Acupuncture Message Transmission

For several years, a number of authors have attempted to scientifically investigate the field of acupuncture, specifically the anatomic relevance of acupuncture points and their connections, known as "meridians."

It has long been known that skin impedance varies significantly in areas related to the classic acupuncture points (1,2). Correlations have also been made between the acupuncture "meridians" and subjective physical sensations in areas of specific dermatological lesions (3).

We have attempted since 1978 to study the migration of radioactive tracers injected at acupuncture points using a scintillation camera coupled to a computer system with image analysis capability (4). Other authors have also examined this subject and obtained reproducible results, including Bagu (5) and Tiberu (6) in Romania, Lafont and Munsch in France and Jia-He Tian and Gu (7) in China. Finally, Dr. S. Kovacs in Barcelona, Spain has obtained similar results in the dog using an identical protocol, as described in this month's issue of the *Journal* (8).

The most commonly used radioactive tracer for these studies has been ^{99m}Tc as sodium pertechnetate. The injection at the acupuncture point, localized with anatomical landmarks, palpation and measurement of local

impedance, is performed with hyperdermic needles of 5/10 mm, at a depth of 3-5 mm, as determined by a specific sensation felt by the subject. The injected volume must be as small as possible, approximately 0.05 ml with an activity of 10-20 MBq.

These efforts have led in two directions: morphological and quantitative dynamic studies. Our work has been conducted in over 250 normal and abnormal subjects. Each experimental protocol has been carefully controlled.

Morphologically, most authors have reported that in analytical studies, a radiotracer injected at a control point shows no preferential migration after 5 min, and only a very slight centrifugal isotropic diffusion around the injection point.

Conversely, when the injection is performed at an acupuncture point, a linear migration is seen from the site of injection. For instance, when the injection is performed at the "Renal 7" acupuncture point (located on the internal side of the leg, above and behind the medial malleolus), the migration distance is 30 cm from the injection point proximally. Such migrations, arising from various acupuncture points located on both the upper and lower limbs, have always been found to follow identical pathways in both control subjects and in patients with various disease.

The pathways thus evidenced are anatomically superimposable with those described in traditional Chinese medicine under the name of "meridians." Twelve meridians are described

in traditional Chinese medicine in the upper and lower limbs. Preferential paths of radiotracer travel are found along these pathways.

Quantitative analyses performed on images and on blood sampled up to 60 min after injection, in both normal and abnormal subjects, show that less than 5% of radiotracer injected at the acupuncture point migrates along the preferential pathway. The remainder of the tracer shows a slow isotropic diffusion from the point of injection. This diffused component of the injected tracer does not produce a sufficient signal to noise ratio to constitute an interpretable image of any linear definable structure such as a vein or lymphatic vessel. However, 15-20 min after injection, uptake appears in organs for which the tracer has a high affinity, such as the thyroid and salivary glands for technetium.

Due to the energy of the ^{99m}Tc gamma photons, it is difficult to visualize the deeper pathway of the meridians in the upper body because of extensive soft tissue attenuation.

Similar results have been obtained using other radioactive tracers, such as ¹³³Xe, ²⁰¹Tl and ¹⁹⁷Hg. In man, no different molecular migratory behaviors between neutral molecules, anions or cations have been shown.

We have tried to establish the uniqueness of the observed pathways and thus eliminate a vascular or lymphatic explanation (9).

Experimental data suggest that these pathways do not correspond with vascular routes. The migration

Received Nov. 13, 1991; accepted Dec. 11, 1991.
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speed along the preferential pathways is slow, approximately 3 to 5 cm/min, and incompatible with vascular transport. In addition, this migration speed is identical whether a radioactive tracer such as [^{99m}Tc]pertechnetate or ¹⁹⁷Hg-bichlorure is used. Renal counts show no significant differences in appearance-time and radioactive concentrations of the two radiotracers, proof that the migration cannot be of vascular origin.

If the tracer injection is performed randomly, partially intravenously, the observed pathway immediately follows the venous route and disappears in less than a minute, while the migration seen along a meridian requires several minutes and disappears slowly over several dozen of minutes. The hypothesis of rapid diffusion towards the vascular bed has also been rejected. The injection of [^{99m}Tc]pertechnetate at the "Liver 3" acupuncture point (next to the dorsal vein of the foot) shows a slow axial pathway of migration conforming to the described meridian, rather than a more rapid and transversely oriented flow as would be expected via the vascular anatomy.

In order to eliminate the hypothesis of a vascular migration, two radiotracers of different energies have been utilized: ^{99m}Tc and ²⁰¹Tl. Technetium-99m was injected at an acupuncture point, ²⁰¹Tl in a vein next to the same acupuncture point.

The images obtained revealed that a meridian pathway is distinct from the vascular pathway. One can see, here again, that the meridian pathway is slow to appear and disappear, whereas the vascular pathway images are immediately constituted and very rapidly fade. This experiment which separates the meridians pathway from the vascular route helps to demonstrate the specificity and uniqueness of these pathways.

In addition, the injection of tracer at point "Gallbladder 36" (located at the mid-calf) frequently reveals migration both retrograde and anterograde on the meridian pathway, incompatible with the vascular migration hy-

pothesis. This same bidirectional migration is found when the injection is performed at other acupuncture points, for example "Stomach 41" at the front of the ankle.

Finally, the injection at point "Large Bowel 18" (located next to the sternocleido-mastoid muscle) on the left, produces a tracer migration toward the upper lip, i.e., in the opposite direction of the venous circulation. This migration crosses the facial median line to reach the region of points "Large Bowel 19 and 20" on the right, located at the nasal base. We have similarly shown that these pathways do not correspond to lymphatic routes.

In order to study the relationship of these pathways to lymphatics, the same dose (20 MBq) and volume (0.05 ml) of [^{99m}Tc]pertechnetate was simultaneously injected at the acupuncture point next to the first interdigital space of the foot, an area for the conduct of isotopic lymphography of the lower limb, the tracer being then used under its colloidal form (rhenium sulfur labeled with ^{99m}Tc).

The "Liver Meridian" is located at this anatomical region, which starts behind the ungueal external angle of the big toe, runs along the external border of this toe to the space between the first and second metatarsal bone on the dorsal side of the foot. This pathway contains two principal acupuncture points: the point "Liver 1", located at the external border of the big toe, next to the transverse depression indicating the junction of the nail and its matrix; and the point "Liver 2", located at the external border of the big toe, in front of the metatarsal phalangeal articulation at the base of the first phalanx, thus at the level of the first interdigital space.

Twenty megabecquerels of ^{99m}Tc were injected at acupuncture point "Liver 2" of the right foot, and simultaneously, an identical dose was injected in the first interdigital space of the left foot, at a similar depth (approximately 3 mm), the needle being slightly oriented outside and down, in

order to avoid as much as possible the liver "meridian".

This produced a clear pattern of tracer migration in the right leg in accordance with the "Liver meridian," originating from the acupuncture point "Liver 2".

However, there is practically no defined migration in the left leg where the injection was performed with the isotopic lymphography technique using a noncolloidal tracer. Conversely, the colloidal tracer injection at an acupuncture point does not produce any migration along the meridian.

A quantitative study was conducted after selecting two mirror regions of identical shape and size on the leg along the "Liver Meridian" pathway, and two similar "background noise" regions outside of the pathways. The counts obtained on the background areas are identical.

There was a great difference in counts in the region of the "Liver meridian" depending on the point of injection: "Liver 2" or interdigital space. The ratio, after normalization and background subtraction is 7.5, in favor of the injection side performed at the acupuncture point.

Later images after one and two hours did not reveal any uptake in the lymphatic nodes of the leg and pelvis, on the side where the injection was performed at acupuncture point "Liver 2", whereas the lymphatic chain appeared on the left side where the injection was performed according to the classical isotopic lymphography technique.

These results suggest that the meridian pathways do not coincide with lymphatic routes, and in the example above, the minimal activity seen in the left leg interdigital space injection (13.5% of right leg) realistically corresponds to a fraction of tracer which has diffused towards the "Liver Meridian."

This morphological study allows us to affirm, contrary to certain authors (10), that the preferential pathways evidenced by radioactive isotopes have unique characteristics, are super-

imposable on the meridians described in traditional Chinese medicine, and are distinguishable from vascular and lymphatic routes.

These pathways may run along the limbs, with the neurovascular bundles. In this manner, according to Bjorn Nordenström from the Karolinska Institute of Stockholm (11), some interstitial spaces would constitute a preferential ionic pathway, corresponding to the meridians known in acupuncture. In addition to the morphological aspect, dynamic and quantitative studies permit us to evaluate migration speed along the pathways (7).

In control subjects and in patients presenting with unilateral renal pathology, two sodium pertechnetate injections of identical volumes and activities are simultaneously performed at acupuncture points "Kidney 7" (at the medial part of the lower leg right and left). The acquisition, starting at injection time, consisting of 128 sequential images of 2, 4 or 8 sec constitutes a dynamic study of radiotracer migration along with the meridian and allows the generation of curves to quantify the evolution of radioactivity in regions of interest located on meridian pathways. For normal subjects, on both sides, the median slopes of the curves are of the same magnitude. Conversely, for a subject presenting with unilateral renal disease, the slopes are very different (12).

It was of interest to us to evaluate the effect of needle stimulation as acupuncture points in the migration of these tracers since such stimulation accounts for the clinical practice of acupuncture. Stimulations were performed at acupuncture points anatomically located proximal or tibial to the radiotracer injection points. Such stimulations were of several types including:

- Mechanical, using other acupuncture needles;
- Electrical, circulating a continuous or alternate electric current between two acupuncture needles.

- Thermic, using a heating stimulation needle, and known in traditional Chinese medicine as "Moxibustion".

To avoid a subjective response from the patient, in some trials we have used a laser beam (produced by a helium-neon tube of 28 MW power) as an agent of stimulation, because it does not provoke any sensation, tactile or thermic. A series of laser stimulations was conducted on healthy subjects.

Two injections of sodium pertechnetate (^{99m}Tc) of identical activity (20 MBq) and volume (0.05 ml) were simultaneously performed at acupuncture points "Kidney 7" right and left (located at the medial side of the leg, above and behind the medial malleolus). The acquisition consisted of 128 sequential images of 8 sec each. In areas of interest defined on the preferential pathways, time-activity curves were constructed.

Eight minutes after injection, a 2-min stimulation was performed unilaterally at the point "Kidney 2" on the left. This point is located on the medial border of the foot, at the lower internal extremity of the scaphoid and first cuneiform articulation.

A marked variation of the tracer's rate of migration was noted simultaneously with stimulation, not only on the stimulation side (left), but also contralaterally (right).

It is known that the efficacy of (low power laser beam) irradiation especially in rheumatology, is best when the beam cutting frequency is low, around 20 Hz. We have found the same applies to the efficacy of laser stimulation of an acupuncture point.

After injection at points "Kidney 7" (right and left), two 2-min unilateral stimulations were conducted, one at the 5th minute at the point "Kidney 2" left, and the other one at the 9th minute at the point "Kidney 2" right. The cutting frequencies were 48 and 24 Hz, respectively. The curves obtained revealed that the 48 Hz stimulation failed to produce a response, whereas a lower cutting frequency (24

Hz) significantly modified the tracer's rate, both uni- and contralaterally, with synchronized change of relatively similar amplitude. A low cutting frequency, around 20 Hz, therefore seems to be optimal to provoke a response to stimulation.

Stimulation trials were conducted after injection at two points of "Large Bowel 4" (right and left) located in the anatomical snuffbox. At the 320th second, an inflated armband was secured at the root of the right arm, at a pressure at least 50% of the systolic arterial blood pressure, and maintained until the 640th second.

During the setting of the armband, a 2-min needle stimulation was performed from the 400th and 520th second, at the point "Large Bowel 11" (located between the injection point and the armband, at the external side of the elbow). The curves revealed a right sided interruption of the tracer's flow, coinciding with the constriction due to the armband, and no response to stimulation. On the left, contralaterally without armband compression, a positive response to stimulation as evidenced by a modification of the tracer's rate was observed.

Thus a constriction constitutes an efficient obstacle to the rate of the tracer in preferential pathways in connective tissues, but does not hinder the contralateral, simultaneous transmission of information.

This contralateral response under constriction is in accord with the classical hypothesis of information transmission by a reflex nervous route, with release of neuromediators (13).

Subsequently, at the biological level, laboratory experiments conducted in collaboration with Doctor Nicolas from the Cytology Laboratory of the Military Hospital of Percy in Paris (14) showed modifications of granulocyte membrane potentials during stimulation of an acupuncture point using either a needle or a laser beam. The cell membrane potential was measured with a fluorometric method on blood sampled 1 min after the end of injections or stimulations,

and compared with control blood from the same subject.

The simple injection of a radioactive tracer at an acupuncture point did not cause any change in the granulocyte membrane potential, compared to control blood. On the other hand, if the stimulation of an acupuncture point did not incur any modifications in the erythrocyte membrane potential, it did cause a statistically significant change in this potential in granulocytes. Finally, no modification of erythrocytes or granulocytes membrane potential was noted when stimulating a placebo point. These findings suggest the ability of acupuncture point stimulation to provoke constant and reproducible changes in cellular physiology.

In conclusion, the migration of a radioactive tracer from one acupuncture point to another, along pathways superimposable with the meridians described by traditional Chinese medicine, taking into account the migration speed and few patterns, does not indicate a intravascular lymphatic origin. These pathways are likely related to connective tissue diffusion following the vascular nervous plexus along the limbs (11).

During the stimulation of acupuncture points, a rapid and simultaneous response is noted in contralateral meridian. As well as on the stimulated side, these responses are identical both in time and in amplitude and duration. This simultaneous contralateral response suggests a neuro-chemical mechanism in information transmission.

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REFERENCES

1. Niboyer J. *Traité d'acupuncture*. In: *Maison-nauve*. Metz:1970.
2. Zhen RR. Luminescence and acupuncture. *Fourth National Symposium of Biophysics*. Beijing, 1983;3:69.
3. The P.S.C. Group. An observation of the phenomena of propagated sensation along the channels. *Symposium of the "Institute of acupuncture and moxibustion Academy of Traditional Chinese Medicine"*. Beijing, China, May 1979.
4. de Vernejoul P, Darras JC, Albarède P, et al. Approche isotopique de la visualisation des méridiens d'acupuncture. *Innov Tech Biol Med* 1984;5-4:465-472.
5. Bagu V, Bugeac G, Vasile A, et al. Aspect préliminaire dans l'étude, à l'aide de la médecine nucléaire, des points d'acupuncture, de la circulation sur les méridiens et leurs rapports avec les organes correspondants. *Congrès international d'acupuncture*. Brno-Tchécoslovaquie 2 Juin 1981.
6. Tiberiu R. Etude des points d'acupuncture par la médecine nucléaire. *Am Acupuncture* 1981; 9-3:251.
7. Gu HS. Etude de la migration de ¹²⁵I au niveau des méridiens. *Chinese J* 1980;3-9:681-682.
8. Kovacs FM, Gotzens V, Garcia A, et al. Experimental study on radioactive pathway hypodermically injected technetium-99m. *J Nucl Med* 1992;33:403-407.
9. de Vernejoul P, Darras JC, Beguin C, et al. Approche isotopique de la visualisation des méridiens d'acupuncture. *Agressologie* 1984; 25:1107-1111.
10. Simon J, Guiraud G, Esquerra JP, Lazorthes Y, Guiraud R. La méthodologie des radioisotopes permet-elle de justifier l'existence des méridiens d'acupuncture? *Bull Acad Natle Méd* 1986;172:363-368.
11. Nordenstöm BEW. *Biologically closed electric circuits*. Uppsala; Nordic Medical Publications; 1983.
12. de Vernejoul P, Albarède P, Darras JC. Etudes des méridiens d'acupuncture par les traceurs radioactifs. *Bull Acad Natle Méd* 1985;169: 1071-1075.
13. de Vernejoul P, Albarède P, Darras JC, Nicolas J, Richardot G, de Vernejoul J. Information transfer approach in acupuncture. In: *Proceedings of the Chinese Academy of Medical Sciences and the Peking Union Medical College International Symposium on Nuclear Medicine*, Peking, China. 10-14 Octobre 1988. 1988;3:65.
14. Richardot G, Darras JC, Nicolas J, de Vernejoul J, Albarède P, de Vernejoul P. Hypotheses sur la transmission du message acupuncturel après stimulation. Etude sur 250 subjects. *XXVIIIème Colloque de Médecine Nucléaire de Langue Française*. Paris, 8-10 December 1988.