Experimental Study on Radioactive Pathways of Hypodermically Injected Technetium-99m

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The objective of this study was to investigate the biological substrate of radioactive pathways of migration of hypodermically injected ^{99m}Tc into points of low electrical resistance. Sixteen anesthetized adult male beagles were used. Control and test points were defined by comparing their electrical resistance to that of the pinna. Seventy-three experiments of three different types were performed: (1) separate hypodermic injections of [^{99m}Tc] sodium pertechnetate, ^{201}Tl-chloride, ^{131}INa and ^{99m}Tc-rhenium sulfide into control and test points; (2) simultaneous injections of [^{99m}Tc]sodium pertechnetate and ^{201}Tl chloride into control and test points; and (3) intravascular injections of $^{99m}TcO_4$ into blood vessels underlying test points. Only the hypodermic injection of ^{99m}Tc into points of low electrical resistance gave rise to a specific radioactive pathway characterized by rapid and longitudinal migration, clearly independent of background activity. The specific radioactive pathway detected is not the result of diffusion of the radiotracer through nerves, veins or lymphatic vessels, but its trajectory coincides with that described for one of the acupuncture meridians in the dog.

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In human beings, hypodermic injection of ^{99m}Tc into points of low electrical resistance gives rise to rapid linear diffusion of the radioactive tracer. The site of these points and the migration pathways coincide with acupuncture points and meridians, respectively (*1–3*). The possibility that these radioactive paths may be the result of lymphatic and vascular drainage of the radioactive tracer is suggested by several authors on the basis of evidence of radioactivity found in venous blood draining the injected area, uptake by target organs (thyroid, salivary glands, stomach), and disappearance of radioactive pathways by compression (*4–6*). Based on anatomical criteria, however, other authors disagree (*7*).

No evidence of any other hypothesis relative to the biological substrate of these radioactive pathways is to be found in the literature. Thus, the purpose of this study was to investigate the presence of radioactive paths in the dog and to assess if diffusion of the radioactive tracer occurs through veins or lymphatic vessels.

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MATERIALS AND METHODS

Sixteen healthy adult male beagles were used in this study. They were preanesthetized using acepromazine maleate (0.2 mg/kg) and atropine sulfate (0.05 mg/kg). Anesthesia was induced using thiopental sodium intravenously (9 mg/kg). Animals were then intubated and anesthesia was maintained using oxygen, nitrous oxide, and halothane.

Control injection points were detected as having the same electrical resistance compared with that of the pinna, where no acupuncture points have been described. They were located on the animal's back and on the dorsal aspect of the animal's metacarpus and metatarsus at least 1 cm distant from the trajectories of acupuncture meridians described for the dog (Darras JC, personal communication) (*8*).

Test injection points were detected as having a lower electrical resistance compared with that of the pinna. These were located on the dorsal aspect of the animal's metacarpus and metatarsus, coinciding with one of the acupuncture meridians described for the dog. Control and test points on the dorsal aspect of the metacarpus and metatarsus were 1.5 cm apart.

A total of 73 experiments were carried out (Table 1). In 58 experiments, a 0.5-mm hypodermic needle was introduced to a depth of 4 mm at a right angle to the skin surface. The absence of blood in the syringe was assessed and a radioactive tracer was injected. Following this methodology, 7.4 MBq of [^{99m}Tc]sodium pertechnetate in a volume of 0.125 ml, 7.4 MBq of ^{131}INa in a volume of 0.05 ml, 11.1 MBq of ^{201}Tl-thallous chloride in a volume of 0.3 ml, and 7.4 MBq of rhenium sulfide in a volume of 0.125 ml were separately injected into both control and test points. In another five experiments following the same methodology, a dose of 7.4 MBq of [^{99m}Tc]sodium pertechnetate in a volume of 0.125 ml with a dose of 11.1 MBq of ^{201}Tl-thallous chloride in a volume of 0.3 ml were injected together into both the control and test points. The remaining 10 experiments consisted of intravascular injections of ^{99m}Tc. A blood vessel underlying a test point was located by needle aspiration and 7.4 MBq of [^{99m}Tc]sodium pertechnetate in a volume of 0.125 ml were injected.

When rhenium sulfide, ^{99m}Tc and ^{201}Tl were injected, the study was performed using an Elscint SP-4 digital gamma-camera with

TABLE 1
Radioactive Tracers and Injection Points in the 73 Experiments

Radiotracer injected	No. injections		
	Metacarpus	Metatarsus	Back
Hypodermic injection:			
Control point			
^{99m}Tc	6	2	8
^{131}INa	3		
^{201}Tl	3		
Rhenium sulfide	5		
^{201}Tl and ^{99m}Tc	3		
Test point			
^{99m}Tc	11	3	
^{131}INa	4		
^{201}Tl	5		
Rhenium sulfide	5		
^{201}Tl and ^{99m}Tc	5		
Intravascular injection:			
^{99m}Tc	5	5	

a low-energy, high-resolution collimator. When ^{131}INa was injected, a high-energy collimator was used. For simultaneous injection of ^{201}Tl and ^{99m}Tc, a dual-tracer acquisition mode was used. In all cases and immediately after injection, acquisition of 1-min consecutive static images were begun using a 128 × 128 matrix word.

The migration of the radioactive tracer from the injection site was assessed visually. In order to obtain a quantification of such migration, the trajectory and diffusion were evaluated after 4 min. The trajectory was divided into segments and its diffusion was calculated using the "x" and "y" coordinates at the furthest points. Measurements obtained in pixels where then converted into millimeters.

RESULTS

In the 63 experiments in which radioactive tracers were hypodermically injected, a "star" effect was immediately observed and radioactivity began to disappear slowly from the injection point as background activity gradually increased. This pattern was noticed after all hypodermic injections of any radioactive tracer into both control and test points.

This was the only pattern observed when the radioactive tracers were injected into the control points. This was also the only pattern observed when ^{201}Tl, ^{131}INa or rhenium sulfide were injected into test points. Therefore, in those cases it was impossible to determine a preferential radioactive trajectory 4 min after injection and even 25 min later no radioactive pathway was observed. However, 90 min after injection of rhenium sulfide at both control and test points, radioactivity in the axillary nodes was detected, although no radioactive pathway was noticed (Figs. 1–7).

On the other hand, in all cases in which ^{99m}Tc was hypodermically injected at a test point, the radioactive tracer moved longitudinally and axially along the anterior surface of the animal's leg. Migration began immediately and was progressive, constant and rapid. Four minutes after injection it had spread up to 109.27 (±3.44) mm (Fig. 8).

In all experiments in which ^{201}Tl was injected together with ^{99m}Tc into a test point, the "star" effect and the simultaneous appearance of the two different patterns were observed, i.e. absence of diffusion of ^{201}Tl and longitudinal, axial and rapid migration of ^{99m}Tc (Fig. 9). However, in all experiments in which both radioactive tracers were injected together into a control point, no migration of either was found (Fig. 10).

The injection of ^{99m}Tc into a blood vessel showed early uptake at the target organs accompanied by a rapid increase in background activity. In this case, a linear migration following the anatomical trajectory of the vessel occurred almost instantaneously (Fig. 11).

DISCUSSION

In the 63 experiments in which radioactive tracers were hypodermically injected, a "star" effect due to concentration of the radioactive agent in a localized area was observed just after injection, and a slow and gradual increase of background activity then was detected. This pattern was probably due to the passive diffusion of radioactive tracers that were slowly reabsorbed and passed into the bloodstream before being taken up by the target organs.

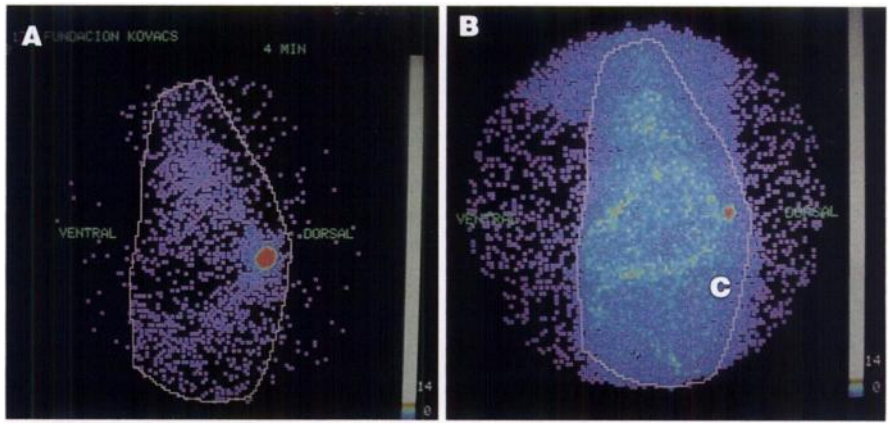

FIGURE 1. Radioactive image obtained 4 min (A) and 25 min (B) after hypodermic injection of ^{99m}Tc into a control point.

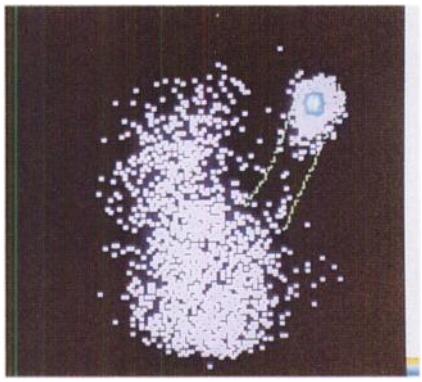

FIGURE 2. Radioactive image obtained 4 min after hypodermic injection of ^{201}Tl into a control point.

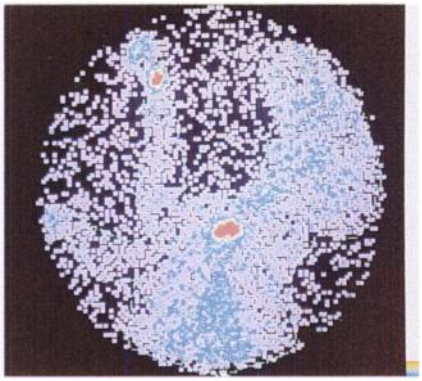

FIGURE 6. Radioactive image obtained 90 min after injection of rhenium sulfide into a control point.

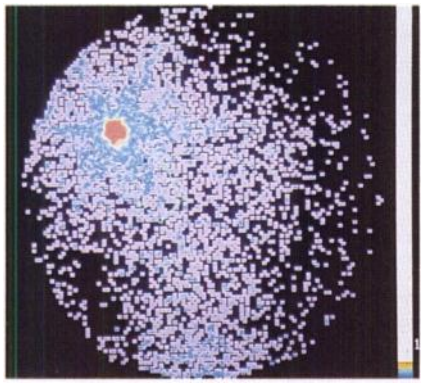

FIGURE 3. Radioactive image obtained 4 min after hypodermic injection of ^{131}INa into a control point.

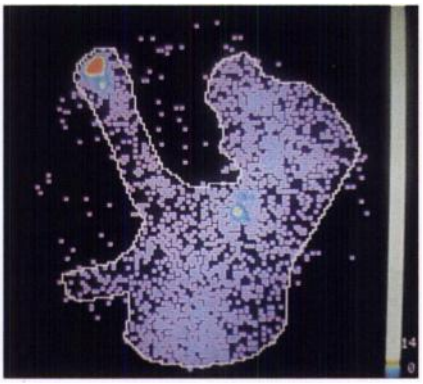

FIGURE 7. Radioactivity detected 90 min after hypodermic injection of rhenium sulfide into a test point.

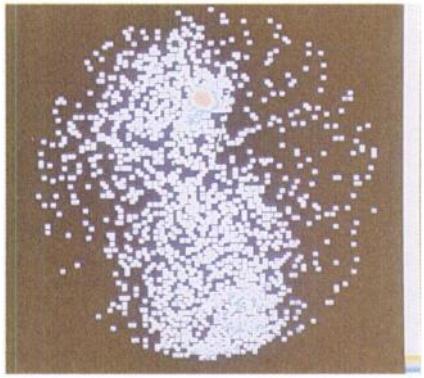

FIGURE 4. Radioactive image obtained 4 min after hypodermic injection of ^{201}Tl into a test point.

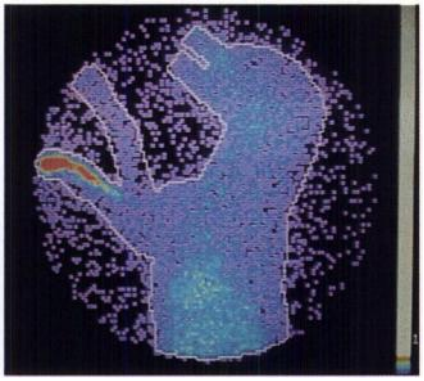

FIGURE 8. Radioactive pathway obtained 4 min after hypodermic injection of ^{99m}Tc into a test point.

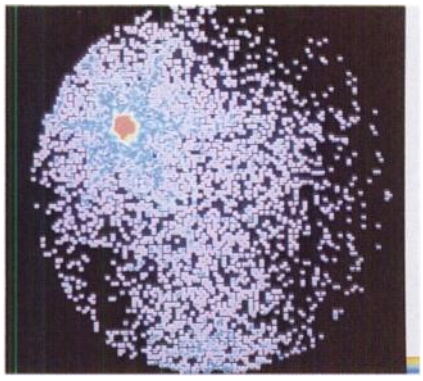

FIGURE 5. Radioactive image obtained 4 min after hypodermic injection of ^{131}INa into a test point.

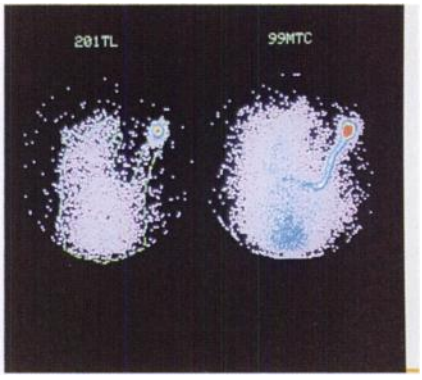

FIGURE 9. Radioactive image obtained 4 min after hypodermic injection of ^{201}Tl and ^{99m}Tc into a test point.

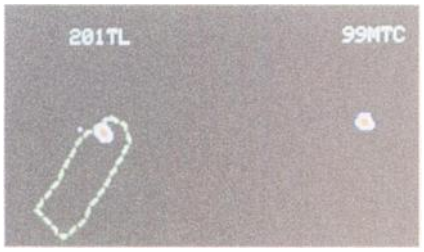

FIGURE 10. Radioactive image obtained 4 min after hypodermic injection of ^{201}Tl and ^{99m}Tc into a control point.

Passive diffusion occurred in all cases after hypodermic injection of radioactive tracers into both control and test points. This could explain the gradual increase in background activity we detected, as well as the increased radioactivity in venous blood draining the injected area and the uptake by target organs found by some authors after hypodermic injection of ^{99m}Tc (*4*,*5*).

This was the only radioactive pattern obtained 4 min after hypodermic injection of all radioactive tracers into a control point and after hypodermic injection of rhenium sulfide, ^{131}INa, and ^{201}Tl into a test point.

However, hypodermic injection of $^{99m}TcO_4$ into a test point gave rise to a second migration pattern characterized by rapid, constant and progressive spread of the tracer, which was clearly different from radioactivity associated with the "star" effect and the gradual increase in background activity. The migration trajectory coincided with that described for one of the acupuncture meridians in the dog (Fig. 12). This radioactive pathway was only observed after ^{99m}Tc being injected into a test point. Neither ^{99m}Tc injected into control points or other radioactive tracers injected into the same test point (even simultaneously) gave rise to such diffusion pattern.

The contribution of vascular elements (arterial, venous or lymphatic) to this specific radioactive pathway has been suggested by some authors. However, the injection of ^{99m}Tc into blood vessels underlying the test points caused a different diffusion pattern, i.e. activity being quickly detected along the anatomical trajectory of the vessel. Because neither the trajectory nor the diffusion speed coincided with those observed after hypodermic injection of ^{99m}Tc, the linear radioactive pathway observed after injection of ^{99m}Tc into points of low electrical resistance cannot be attributed to the passage of the radioactive tracer through the blood vessels.

FIGURE 12. Acupuncture meridian described in the dog (Darras JC, personal communication) (*8*).

An explanation for linear radioactive pathway by diffusion of ^{99m}Tc through lymphatic vessels was also excluded, because after injection of rhenium sulfide, a specific tracer for lymph node detection, no clear path or trajectory could be observed and only late radioactivity in the lymph nodes corresponding to the injected area was found. This diffusion pattern was the only one detected after injection of rhenium sulfide in both test and control points and was different from that observed after injection of ^{99m}Tc.

In addition, when ^{201}Tl and ^{99m}Tc were injected together into a test point, the linear migration pattern already described was only observed for ^{99m}Tc. This fact also negates explanation of a linear migration pattern through lymphatic or vascular drainage of the radioactive tracer.

Migration of ^{99m}Tc through nerve fibers can be excluded since the radioactive path does not coincide with any anatomical structure of this type nor does the diffusion speed suggest this either. Moreover, no evidence is available to show that ^{99m}Tc has affinity for nerve tissues.

In conclusion, at present no anatomical or physiological substrate is known to be responsible for specific radioactive pathways in experimental animals injected with ^{99m}Tc into cutaneous points where electrical resistance is low. Further studies are needed to clarify this specific spread pattern and to determine its eventual biological substrate and significance.

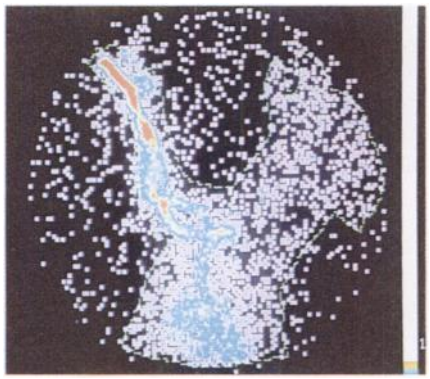

FIGURE 11. Visualization of the cephalic vein 10 sec after injection of ^{99m}Tc into a blood vessel.

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EDITORIAL

Anatomic Divisions

Most western physicians, with mixed to negative feelings, relegate acupuncture to the perjorative world of "alternative medical practices." This reflects both responsible clinical conservativism and scientific disdain for the credulous. Acupuncture was little known in the west until James Reston's 1971 account of his appendectomy in China. Since then, increasingly reliable reports have suggested its value in circumscribed areas of medical practice, particularly those related to pain management. Unfortunately, most curious physicians have neither the time nor expertise to verify these methods for themselves. They must instead rely upon secondhand data to validate a medical system whose tenets are at odds with western models of physiology and disease causation.

Just recall, four years ago, a startling report that appeared in the pages of *Nature*. The authors claimed that extremely dilute suspensions of IgE antibody, so dilute that no IgE molecules were even statistically present, caused basophil degranulation (*1*). Accompanied by an assurance of editorial incredulity, this paper prompted formal attempts at "debunking" (*2–3*) and much dissension in the scientific community. Rejoicing homeopaths envisioned the scientific validation of their methods, while mainstream scientists were infuriated at this "lapse" in a prestigious journal. The dispute was at least as interesting as were the effective, but absent, IgE molecules.

This paper was more than just another piece of the jigsaw. It assaulted one's sense of reality and broke the agreement as to what constitutes a reasonable act on the part of nature. This tacit understanding allows us to design experiments and interpret data. It does not appear in the methods section nor in the discussion, nor is it controlled for by statistical analysis. Without this agreement as to what is reasonably real, our scientific efforts would be as doomed as Babel. Yet even the necessary weltanschauung tends toward ossification. Respected scientists have passed cursory judgments on matters outside their purview on the grounds of inconsistency with preestablished world views. How many of us believe in astrology and on the basis of what evidence? Are we likely to have similar predispositions toward the interpretation of thallium washout rates? Too often, it is not the quality of our work but its orthodoxy that determines how we will be regarded by our peers. Charles McCutcheon suggests that the cooperation of referees with the establishment forces a "deadening uniformity" and serves to "force innovators into the arms of the establishment" (*4*). The authors of the article in *Nature* crossed that political "line in the desert" that separates the real from the imagined. On the other side stand a large number of lunatics and fools, with a smaller contingent of the courageous and innovative.

This reality sense constitutes, from a Bayesian perspective, an a priori probability. A heavily weighted prior probability requires stronger evidence to contradict than does a weak one. Yet the production of such convincing evidence is a time- and resource-intensive task for the research establishment. Is the investigation of such alternative hypotheses worth the cost in view of their presumably low chances of success?

Certainly it is not unless provocative evidence justifies this investment. Acupuncture, a discipline within the larger field of both traditional Chinese and Tibetan medicine, carries a several-thousand year tradition of practice. This longevity alone bears some validity as testimonial. The concept of controlled studies (as we understand them), however, is a new one in traditional Chinese medicine. Anecdotal evidence by reliable observers (*5–6*) has encouraged preliminary efforts in this direction, but there is still disagreement as to whether the effort is justified, given competing demands made upon the research establishment.

Recently, there has been a good deal of public attention paid to these traditional "eastern" medical models. Most interest has centered around Ayurveda (*7*) (an Indian tradition), Tibetan (*8*) and traditional Chinese

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