

## Nuclear Medicine Methods in the Assessment of Acupuncture Effects: A Short Review

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### ABSTRACT

*The mechanisms of acupuncture are poorly understood. In consequence, numerous investigators have conducted clinical trials to test the efficacy of acupuncture in various conditions. We have used PubMed database system to evaluate the number of publications in acupuncture and nuclear medicine procedures in the period from 1964 to 2007, using the keywords: "nuclear medicine and acupuncture", "SPECT and acupuncture", "PET and acupuncture", "scintigraphy and acupuncture", "radionuclide and acupuncture", "radiopharmaceutical and acupuncture", "radioisotope and acupuncture" and "<sup>99m</sup>Tc and acupuncture". Some papers published in English language were selected and a short review is presented. The analysis of the number of publications shows that when a method is well accepted by the scientific community, as the methods used in nuclear medicine, the interest in the development of research increases. Moreover, important findings are presented when the nuclear medicine image is used to evaluate the effect of the acupuncture.*

**Key words:** Acupuncture, nuclear medicine, Traditional Chinese Medicine

### INTRODUCTION

In nuclear medicine, radionuclides such as technetium-99m (<sup>99m</sup>Tc) are widely used to label molecular and cellular structures (radiopharmaceuticals). The radiopharmaceuticals are utilized to study blood flow, metabolism, morphology of an organ or system (Chandra, 1998) and to evaluate the drug formulation and drug delivery systems (Perkins and Frier, 1999). Scintigraphic images using single photon emission computerized tomography (SPECT) and/or

positron emission tomography (PET) which demonstrate the physiological processes of a tissue, allow measurement of physiologic processes as well as alterations related to various diseases (Hladik III et al., 1987; Early and Sodee, 1995; Saha, 2004). The availability of sophisticated imaging methods such as SPECT and PET, as well as in vitro experimental assays (Senna-Fernandes et al., 2006; Souza et al., 2007), have prompted their use to study techniques used in the Traditional Chinese Medicine (TCM), as

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acupuncture (Newberg et al., 2005; Campbell, 2006).

Recent interest in complementary and alternative medicine has promoted research on various procedures for healing and health care (Kawakita et al., 2006). The TCM is a system that deals with the physiology and pathology, as well as diagnosis, prevention and treatment of disease. The TCM considers the body, the man and the nature world as an inseparable whole. Using the method of synthetic analysis, TCM, on the macroscopic point of view, studies dynamic intrinsic relationships of the body and the relationship between interior and exterior environment and then makes clear the basic physiology to serve medical practice (Zhixian, 2003).

The general theory of TCM is based on the premise that there are patterns of energy flow (qi) through the body that are essential for health and several techniques, as acupuncture, phytotherapy, moxabustion and qigong use this approach. Disruptions of this flow are believed to be responsible for several diseases. Acupuncture describes a family of procedures involving the stimulation of anatomical locations on the skin by thin, solid and metallic needles, which are manipulated manually or by electrical stimulation (Ramsay and Greenman, 1998; Sugai et al., 2004; Takahashi, 2006).

In TCM, internal organs (*zang-fu organs*) are divided into three groups: (a) five *zang* organs, (b) six *fu* organs, and (c) extraordinary organs. The five *zang* organs include the heart (including pericardium), lung, spleen, liver and kidneys; their functions are stated mainly to produce and store essence: *qi*, blood and body fluid. The six *fu* organs refer to the gallbladder, stomach, large intestine, small intestine, urinary bladder and *san-jiao* (tri-heater or triple energizer); their functions are anecdotally cited to receive and digest food, to absorb nutritive substances, to transmit and excrete waste. The extraordinary organs are regarded as extra *fu*-organs, including the brain, marrow, bone, vessels, gallbladder and uterus. However, their functions are similar to those of the *zang* organs (Chen, 1998; Yamamura, 2001).

The mechanisms of acupuncture are still poorly understood. In consequence, several investigators have conducted clinical trials to test the efficacy of acupuncture for various conditions (Moffet, 2006). Various methods, as the used in nuclear medicine and radiopharmacy with clinical or basic

approaches, have been utilized to try to obtain scientific evidences about the techniques used in TCM (Yin et al., 2003; Schlunzen et al., 2007).

The interest of the scientific community in a specific subject can be evaluated by the analysis of the number and quality of published papers in journals that are indexed in database system, as in PubMed. Therefore, the aim of this study was to use the PubMed database system to evaluate the number of publications with the techniques of acupuncture, and to compare these findings with the publications in nuclear medicine. Moreover, short review and a discussion of some published papers in English involving acupuncture and techniques with radiopharmaceuticals found in PubMed are also presented.

## MATERIALS AND METHODS

The searches were performed in PubMed (<http://www.ncbi.nlm.nih.gov/PubMed>) in the period 1964 to 2007 using the keywords: (i) "nuclear medicine and acupuncture", (ii) "SPECT and acupuncture", (iii) "PET and acupuncture", (iv) "scintigraphy and acupuncture", (v) "radionuclide and acupuncture", (vi) "radiopharmaceutical and acupuncture", (vii) "radioisotope and acupuncture" and (viii) "<sup>99m</sup>Tc and acupuncture" in the link (<http://www.ncbi.nlm.nih.gov:80/entrez/query.fcgi?CMD=search&DB=PubMed>). The data were obtained in July 4<sup>th</sup> 2007. The number of publications, in each year, was determined in acupuncture, nuclear medicine, SPECT, PET, scintigraphy, radionuclide, radiopharmaceutical, radioisotope and <sup>99m</sup>Tc. The total number of citations in each subject in the studied period was also determined. We have selected some papers published in English to further discussion

## RESULTS AND DISCUSSION

In general, a small number of publications related with the studied subjects was found. The PubMed search, using the keywords (i) "nuclear medicine and acupuncture" yielded 30 publications; (ii) "SPECT and acupuncture" yielded 9 articles, (iii) "radionuclide and acupuncture" were 50 articles, (iv) "scintigraphy and acupuncture" were 33 articles, (v) "PET and acupuncture" were 19

articles, (vi) “radiopharmaceutical and acupuncture” were 0 articles, (vii) “radioisotope and acupuncture” were 16 articles and (viii) “ $^{99m}\text{Tc}$  and acupuncture” were 11 articles.

Numerous reports on the miracle success of various surgical operations with acupuncture needling surprised clinicians and basic researchers throughout the world, and the analgesic effect of acupuncture needling became the initial target of investigation (Kawakita et al., 2006).

After reviewing some recent studies involving acupuncture and nuclear medicine in humans, they

were analyzed according to their intervention, method of the nuclear medicine used, and the diagnostic or treated characteristic (table 1). Recent (from 2001) articles published in English were included in this short review.

Moreover, some studies involving acupuncture and nuclear medicine in animals were also analyzed according to their intervention, nuclear medicine procedure, and the diagnostic or treated characteristic (table 2).

**Table 1** - Some recent studies involving acupuncture and nuclear medicine in humans.

Study	Intervention	Nuclear medicine method	Diagnostic or treated characteristic
Schlunzen et al., 2007	Stimulation of acupoint <i>Hegu</i> (LI4)	PET	Cerebral blood flow in healthy humans
Wong et al., 2006	Body acupuncture	PET	Brain glucose metabolism in cerebral palsy
Ha-Kawa et al., 2006	Body acupuncture	SPECT	Cerebral blood flow in dystonia
Newberg et al., 2005	Acupuncture analgesia	SPECT	Cerebral blood flow in chronic pain
Yin et al., 2003	Stimulation of acupoint <i>Zusanli</i> (ST36)	PET	Brain function in healthy humans
Lee et al., 2003	Stimulation of acupoints LI4, <i>Shousanli</i> (LI10), <i>Quchi</i> (LI11), <i>Jianyu</i> (LI15), <i>Jugu</i> (LI16) and <i>Waiguan</i> (TE5)	SPECT	Cerebral blood flow in stroke
Hsieh et al., 2001	Stimulation of acupoint LI4	PET	Analgesic effect

**Table 2** - Some recent studies involving acupuncture and nuclear medicine in animals.

Study	Intervention	Nuclear medicine procedure	Diagnostic or treated characteristic
Souza et al., 2007	Stimulation of acupoint <i>Sanyinjiao</i> (SP6) in <i>Wistar</i> rats	Bioavailability of radiopharmaceutical sodium pertechnetate	Uptake of the radiopharmaceutical in organs
Senna-Fernandes et al., 2006	Stimulation of acupoint ST36 in <i>Wistar</i> rats	Bioavailability of radiopharmaceutical sodium pertechnetate	Uptake of the radiopharmaceutical in organs
Choi et al., 2002	Electroacupuncture stimulation of acupoint ST36 in <i>Sprague-Dawley</i> rats	Radiolabeled of cells with $^{51}\text{Cr}$	Splenic natural killer cell activity

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” (De Vernejoul et al., 1992). Acupuncture has been used in the treatment of

pain for over 2300 years in China (Zhixian, 2003) and is firmly established as a method of pain control.

The development of experimental models to help understanding the possible mechanism of action of the stimulation of acupoints is worthwhile. In nuclear medicine, a radiopharmaceutical presents a normal bioavailability that might be altered due to diseases and this fact is important to define the diagnosis of a disorder. Protocols that evaluate the bioavailability of radiopharmaceuticals have permitted to investigate the influence of certain synthetic drugs (Gomes et al., 2002; Jankovic and Djokic, 2005), natural products (Moreno et al., 2004), physical exercises (Llaurado et al., 1981; Ollenberger et al., 1998) and stimulation of acupuncture points (Senna-Fernandes et al., 2006; Souza et al., 2007).

Occasionally, unconventional forms of treatment can cause unexpected results when modern diagnostic procedures are applied, as occurred with the patient in the study of Kuno and Cerqueira (1995). A man with back pain was referred for a bone scintigraphy, and the images of the skull showed increased uptake in several regions of the skull, upon questioning, the patient stated that he had received acupuncture treatment for his back pain several times in the same regions as the increased uptake. They suggested that acupuncture can cause enhanced bone metabolism demonstrated by increased activity on bone scintigraphy. These findings are important due to an inadequate interpretation of the nuclear medicine image could lead to misdiagnosis or the necessity to repeat the examination increasing the radiation dose to the patient and staff (Hladik III et al., 1987; Bernardo-Filho et al., 2005).

Newberg et al. (2005) investigated the cerebral blood flow changes associated with the analgesic effect of acupuncture in patients with chronic pain. The baseline scintigraphy of the pain patients showed significant asymmetric uptake in the thalami compared to controls. This asymmetry reversed or normalized after the acupuncture therapy. The results from these cases show that hexamethyl propyleneamine oxime (HMPAO)-SPECT is capable of detecting changes in cerebral blood flow associated with pain and that acupuncture analgesia is associated with changes in the activity of the frontal lobes, brain stem, and thalami.

The use of models to study the interactions between acupuncture stimulation and

bioavailability of radiopharmaceuticals labelled with  $^{99m}\text{Tc}$  may help to understand the potential actions of acupuncture points in different organs and tissues. Senna-Fernandes et al. (2006) have shown that the stimulation of the acupuncture point *Zusanli* (ST36) has increased the uptake of the radiopharmaceutical  $^{99m}\text{Tc}$  - sodium pertechnetate ( $\text{Na}^{99m}\text{TcO}_4$ ) in some organs (heart, spleen, pancreas, stomach, brain and testis) from *Wistar* rats, and Souza et al. (2007) showed that stimulating the *Sanyinjiao* (SP6) point, the bioavailability of  $\text{Na}^{99m}\text{TcO}_4$  was significantly altered in the small intestine.

The PET imaging of brain function in the study of Yin et al. (2003) showed increase in the glycometabolism in the hypothalamus, head of the caudate nucleus, temporal lobe, the sinistral cerebellum, postcentral gyrus, and brain stem while the acupoint ST36 was being punctured. Moreover, the study of Schlunzen et al. (2007) showed that the manual acupuncture stimulation of LI4 point demonstrated a significant decrease in regional cerebral blood flow in the right medial frontal gyrus and in the left putamen measured with PET.

A repercussion of scientific work depends on the quality and the reputation of the journal where the paper is published. These journals are indexed in databases, as PubMed, and, in general, are available, as abstract or full paper to the scientific community (Moffet, 2006) and are also used as a tool to study the interest in some subjects (Santos-Filho et al., 2003). The analysis of the results (table 1 and table 2) shows that when a method is well accepted by the scientific community, as the methods used in nuclear medicine, the interest in the development of research increases. Moreover, important findings are presented in this work when the nuclear medicine image is used to evaluate the effect of the acupuncture.

## CONCLUSIONS

Understanding the physiologic basis of acupuncture may be critical to producing reproducible results. However, the effects of acupuncture must be mediated through physiology and investigators should be able to suggest some possible mechanisms. Proposing and testing ideas about the underlying mechanisms of acupuncture could eventually lead to a real understanding about how acupuncture does work. Furthermore, the

publications found in the PubMed have aided to evaluate the scientific interest in acupuncture and in nuclear medicine.

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## RESUMO

Os mecanismos de ação da acupuntura ainda não são completamente esclarecidos. Em consequência, diversos pesquisadores têm conduzido testes clínicos para verificar a eficiência da acupuntura em condições diversas. Nós utilizamos o sistema de base de dados PubMed para avaliar o número de publicações em acupuntura e procedimentos em medicina nuclear no período de 1964 até 2007, usando as palavras-chaves: “medicina nuclear e acupuntura”, “SPECT e acupuntura”, “PET e acupuntura”, “cintilografia e acupuntura”, “radionuclídeo e acupuntura”, “radiofármaco e acupuntura”, “radioisótopo e acupuntura” e “<sup>99m</sup>Tc e acupuntura”. Alguns artigos publicados em inglês foram selecionados e uma pequena revisão é apresentada. A análise do número de publicações mostra que quando um método é bem aceito pela comunidade científica, como os métodos utilizados em medicina nuclear, o interesse em desenvolver novos estudos aumenta. Além disso, importantes achados são apresentados quando a imagem da medicina nuclear é utilizada para avaliar o efeito da acupuntura.

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