

## The New BBB Indicator of Positron Emitting Radionuclide Tracer - $^{45}\text{Ti}$ -DTPA

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<sup>45</sup>Ti-DTPA

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Positron emission computed tomography combined with cyclotron produced positron emitting radionuclide tracers have given great impacts not only on the clinical diagnosis but also on the various physiological investigations of human beings. Only this newly developed equipments made it possible to show many in vivo physiological changes clearly as a three dimensional, topographic image with quantifiable data. The purpose of this study is to investigate the usefulness of a newly synthesized positron emitting radionuclide tracer - <sup>45</sup>Ti-diethylene-triaminepentaacetic acid (DTPA) as a possible blood brain barrier (BBB) indicator on positron emission computed tomography using an autoradiographic technique.

Method

<sup>45</sup>Ti-DTPA<sup>3)</sup> 3-5 mCi and 2 % Evans Blue (2 ml/kg) were injected intravenously to anesthetized Wistar rats. Fifteen minutes later, hypertonic mannitol solution 2.5 ml was infused through the external carotid artery into the internal carotid artery so as to destroy BBB according to the method of Pappius et al.<sup>4)</sup>. Thirty minutes after the infusion of mannitol, animals were decapitated and the frozen brains were sectioned 30 μm thickness in a cryostat with taking photographs of Evans Blue stained brain sections. The sections were then exposed to the X-ray film to get the image of <sup>45</sup>Ti and was compared to the Evans Blue stained image. Also at the time of sacrificing animals, blood samples were taken to examine the distribution of <sup>45</sup>Ti in the serum by high performance liquid chromatography (HPLC).

Results

In all animals showing a hemispheric BBB destruction, the two images of <sup>45</sup>Ti-DTPA and Evans Blue looked similar each other (Fig. 1). Also the radioactivity of <sup>45</sup>Ti in the serum was found in the albumin fraction (Fig. 2).

Discussion

The conventional BBB indicator on positron emission computed tomography - <sup>68</sup>Ga-EDTA - has been used in various studies and proved useful to determine the regional failure of BBB functions<sup>1)</sup>. However, this tracer has several problems; it is commercially available as a generator form but cannot be produced by in-house cyclotron, and it has been known to have break through phenomenon of <sup>68</sup>Ge (T 1/2 = 280 days) from the generator. We cannot deny the possible hazard of

this long lasting radionuclide existing in the body even though it is a tracer dose. As compared to  $^{68}\text{Ga}$ -EDTA, newly synthesized  $^{45}\text{Ti}$ -DTPA having a sufficiently short half life of 3.09 hr is producible by in-house cyclotron and is free from other radioactive contaminants of long half lives.

As reported before<sup>3)</sup>,  $^{45}\text{Ti}$ -DTPA presents in the blood at high level and retains for somewhat long time. This character seems an essential factor as a BBB indicator. The results of HPLC analysis indicates that  $^{45}\text{Ti}$ -DTPA combines with albumin in the serum and extravasates when BBB was destroyed as same as Evans Blue does<sup>2)</sup>.

Our results indicate that  $^{45}\text{Ti}$ -DTPA would become available as a BBB indicator on positron emission computed tomography in the very near future.

#### Acknowledgment

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#### References

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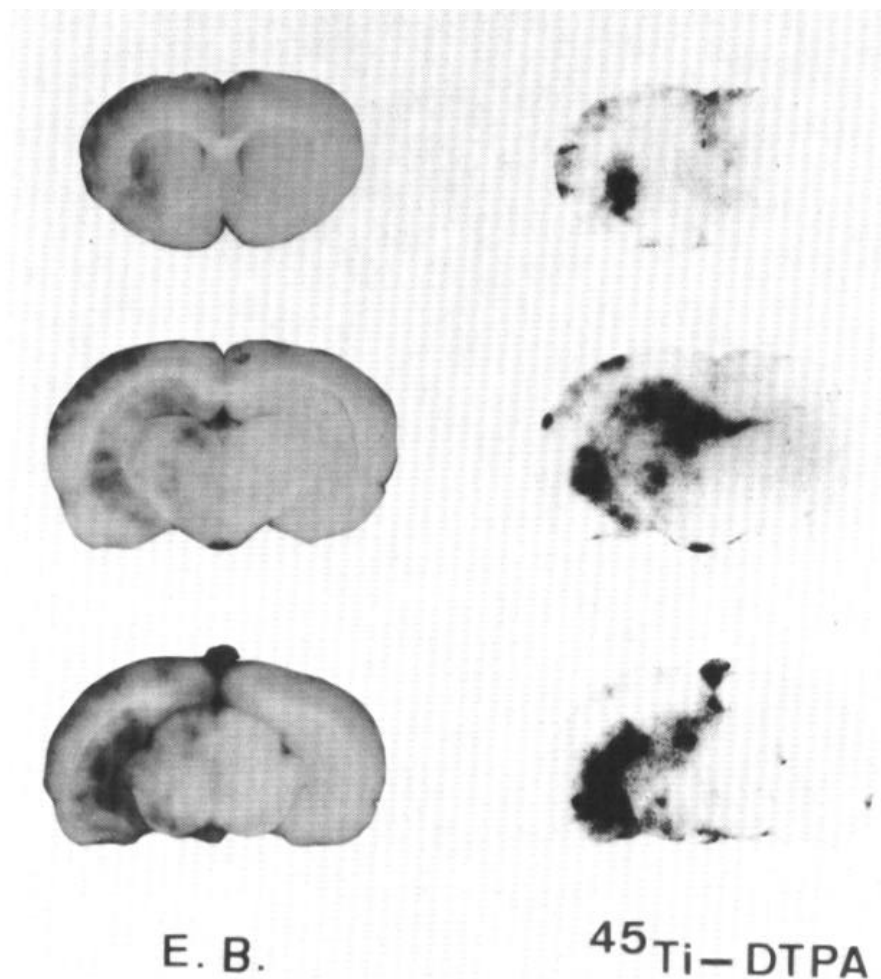


Fig. 1.  $^{45}\text{Ti}$ -DTPA autoradiography and Evans Blue stained image from the identical brain sections.  
Two distribution images looked similar each other.

HPLC OF RAT SERUM AFTER INJECTION  
OF  $^{45}\text{Ti}$ -DTPA

Column : G3000SW 0.75×60cm  
Eluent : 0.15M NaCl, 20mM acetate buffer, pH5.9  
Flow Rate : 1 ml/min

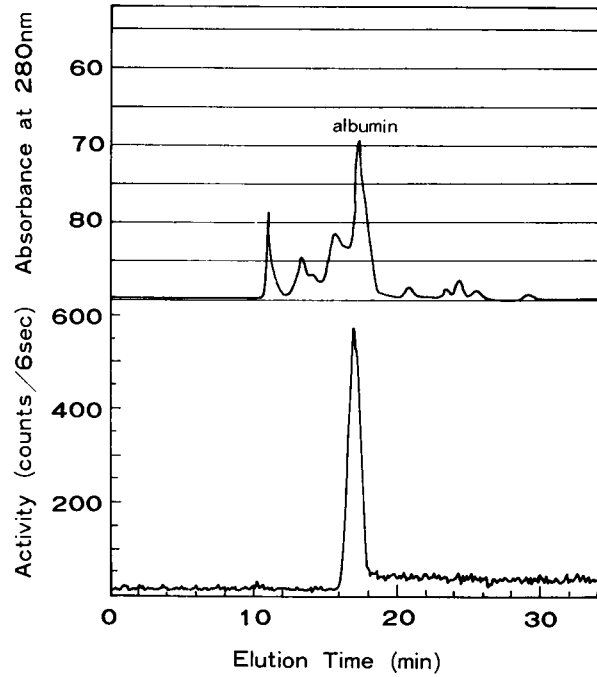


Fig. 2. HPLC elution profile of  $^{45}\text{Ti}$  in the serum.  
The radioactivity peak of  $^{45}\text{Ti}$  was found in the albumin fraction.