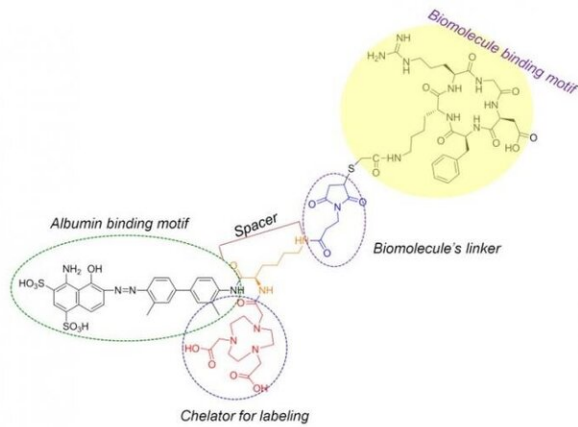
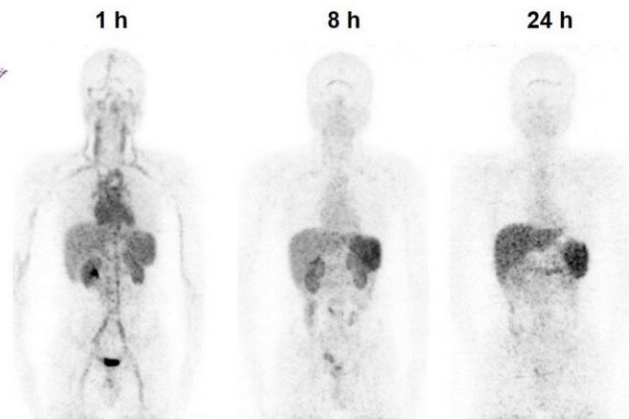


New PET radiotracer proven safe and effective in imaging malignant brain tumors

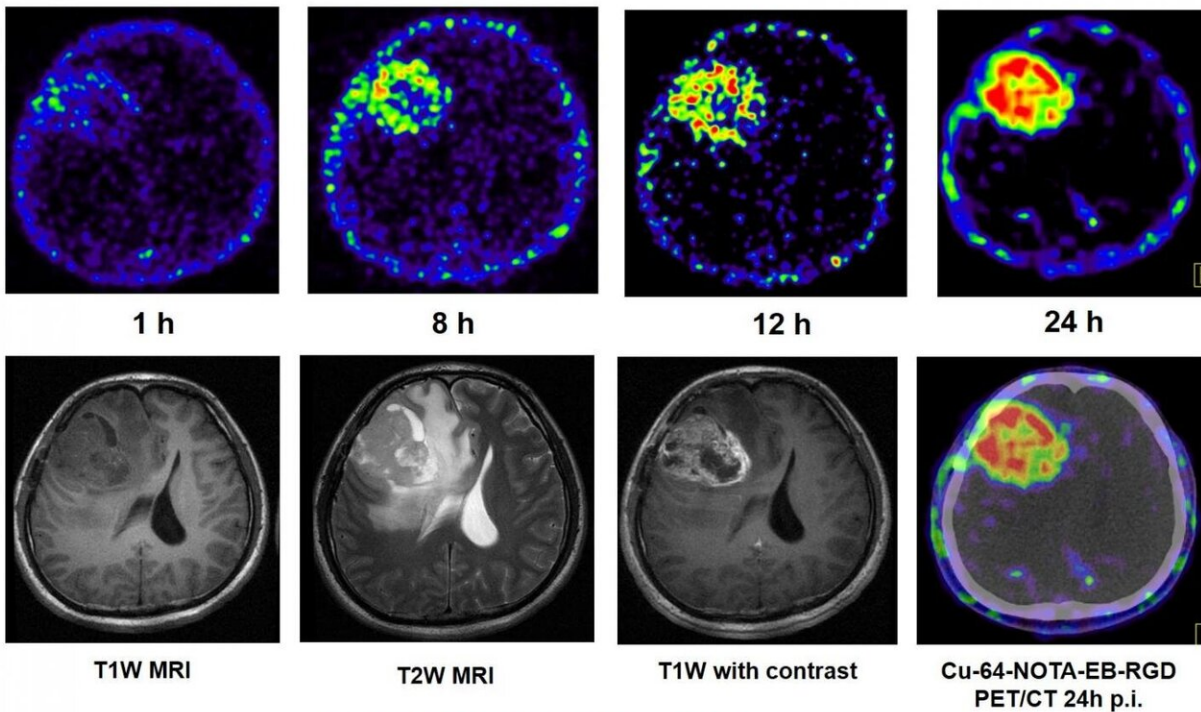
July 13 2020



Chemical structure of NOTA-EB-RGD



Cu-64-NOTA-EB-RGD in healthy volunteers



Cu-64-NOTA-EB-RGD in GBM patients

Representative maximum-intensity projection PET images of a healthy human volunteer injected with ^{64}Cu -NOTA-EB-RGD at 1, 8, and 24 hours after injection. Axial MRI and PET slices of glioblastoma patient injected with ^{64}Cu -NOTA-EB-RGD at different time points after injection. Credit: Jingjing Zhang et al., Peking Union Medical College Hospital, Beijing, China/Xiaoyuan Chen et al., Laboratory of Molecular Imaging and Nanomedicine, NIBIB/NIH, Bethesda, USA

A first-in-human study presented at the Society of Nuclear Medicine and Molecular Imaging 2020 Annual Meeting has demonstrated the safety, favorable pharmacokinetic and dosimetry profile of ^{64}Cu -EBRGD, a new, relatively long-lived PET tracer, in patients with glioblastomas. The radiotracer proved to be a superior, high-contrast imaging diagnostic in patients, visualizing tumors that express low or moderate levels of $\alpha v\beta 3$ integrin with high sensitivity.

Glioblastoma is the most common and most aggressive primary malignant brain tumor in adults, with 17,000 diagnoses annually. It is a highly diffuse and invasive disease that is personally devastating and virtually incurable. Once diagnosed, most patients survive less than 15 months, and fewer than five percent survive five years.

The ^{64}Cu -EBRGD radiotracer presented in this study has several unique qualities. The peptide sequence Arg-Gly-Asp (RGD) specifically targets the cell surface receptor $\alpha v\beta 3$ integrin, which is overexpressed in glioblastomas. To slow clearance, Evans Blue (EB) dye, which reversibly binds to circulating albumin, is bound to RGD, significantly enhancing target accumulation and retention. The addition of the ^{64}Cu label to EBRGD provides persistent, high-contrast diagnostic images in glioblastoma patients.

This first-in-human, first-in-class study included three healthy volunteers who underwent whole-body ^{64}Cu -EBRGD PET/CT. Safety data—including vital signs, physical examination, electrocardiography, laboratory parameters and adverse events—were collected after one day and after one week. Regions of interest were drawn, time-activity curves were obtained and dosimetry was calculated. Two patients with recurrent glioblastoma also underwent ^{64}Cu -EBRGD PET/CT. Seven sets of brain PET and PET/CT scans were obtained over two consecutive days. Tumor-to-background ratios were calculated for the target tumor lesion and normal brain tissue. One week after radiotracer administration, the patient underwent surgical treatment, and immunohistochemical staining of tumor samples was performed.

^{64}Cu -EBRGD was well-tolerated in patients with no adverse symptoms immediately or up to one week after administration. The mean effective dose of ^{64}Cu -EBRGD was very similar to the effective dose of an ^{18}F -FDG scan. Injection of ^{64}Cu -EBRGD to the patients with recurrent glioblastoma showed high accumulation at the tumor with continuously increased tumor-to-background contrast over time. Post-operative pathology revealed World Health Organization grade IV glioblastoma, and immunohistochemical staining showed moderate expression of the $\alpha\text{v}\beta\text{3}$ integrin.

"In this study, we have demonstrated a potential radiotheranostic agent that is safe, sensitive and highly selective in humans, which infers a future diagnostic tool and breakthrough targeted radiotherapy for [glioblastoma patients](#)," said Jingjing Zhang, MD, Ph.D., of Peking Union Medical College Hospital, Beijing, China. "We believe this innovative use of ^{64}Cu -EBRGD will significantly improve therapeutic efficacy and patient outcomes."

" ^{64}Cu -labeled EBRGD represents a viable model compound for therapeutic applications since ^{177}Lu , ^{90}Y or ^{225}Ac can be substituted

for ^{64}Cu ," said Deling Li, MD, of Beijing Tiantan Hospital, Capital Medical University, Beijing, China. "We are currently studying the ^{177}Lu homolog to treat [glioblastoma](#) and other $\alpha v \beta 3$ integrin expressing cancers, including non-small cell lung, melanoma, renal and bone, and hope to build on the current wave of radiotherapies like ^{177}Lu -DOTATATE."

Provided by Society of Nuclear Medicine and Molecular Imaging

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