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Treatment outcome in patients treated with single-dose irradiation (SDRT) for oligometastatic disease

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Purpose: to analyze treatment outcome following Single-Dose Image-Guided Radiotherapy (SDRT) using PERCIST criteria based on 18-F-fluoro-2-deoxy-D-glucose PET Standardized Uptake Value (SUV_{max}) assessments in patients with limited extra-cranial metastatic disease.
Methods and Materials: 259 lesions in 101 consecutive patients with early metastatic disease with less than five lesions at initial presentation (mean 2.1, range 1-5 lesions) were treated between November 2011 and March 2015 with SDRT. Mean and median PTV volume were 40.6 and 18.1 cm^3 (range, 1.3-339), respectively. PTV prescription dose was 24Gy. Of the 101 patients, 56 (55%) of had a solitary metastasis at the time of first treatment. While the majority of the patients received only one treatment, 27% (27/101) received additional treatments (mean 1.4, median 1 range, 1-7) for relapses elsewhere. Thus, the mean number of lesions for the entire population was 2.6 (range, 1-13). SUV_{max} were acquired at the time of FDG-PET/CT planning before SDRT, at 3 and 6 months post-treatment and every 6 months thereafter. Treatment outcome was assessed by PERCIST criteria, with metabolic relapse defined as any increase of SUV_{max} >20% above nadir level. All metabolic relapses were confirmed by morphologic imaging. Lesions had a minimum of 2 post-treatment scans (mean 4; range 2-11) with a minimum follow-up of 6 months.
Results: actuarial 2- and 3-year overall survival for this cohort were 71% and 64%, respectively. At a median follow-up of 16.1 months (range, 6.7- 43.5 months), 6% (15/259) of lesions developed PERCIST failure within the irradiated region yielding a 3-year actuarial freedom of local relapse of 90%. Mean time to local relapse was 9 months. All recurrences occurred within the first 19 months. The mean percentage increase in SUV_{max} in relapsing lesions was 429% (range, 28% - 2530%). The mean and median baseline SUV_{max} were 8.9 and 6.9, respectively (range, 0.7-52.0). At 3 months post-SDRT, 15% (40/259) of the lesions had a >90% reduction in SUVmax (PERCIST complete metabolic response). SUV_{max} declines >75% ($\Delta SUV_{max\ >75\%}$) was significantly associated with freedom from metabolic relapse at 3 years ($p = 0.02$). Lesions with with $\Delta SUV_{max\ >75\%}$ had 94% local control at 36 months *vs*. 77% for $\Delta SUV_{max\ \leq 75\%}$. On univariate analysis, no correlation was found with primary tumor histology, metastasis site, PTV volume or ongoing systemic treatment and the likelihood of local relapse free survival.
Conclusion: These results confirm that high dose SDRT provides long-term local relapse-free survival using objective PERCIST therapeutic response criteria in patients with early metastatic disease. Additionally, they provide preliminary evidence that an early evaluation in metabolic changes post-SDRT may serve as a useful prognostic tool in the assessment of lesions treated with ablative intent.

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How to produce scandium-44 efficiently?

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Purpose: Among the large number of radionuclides of medical interest, Sc-44 is promising for PET imaging. Either the Sc-44g or the Sc-44m can be used for such applications, depending on the molecule used as vector. This study compares the production rates of both Sc-44 states, when protons or deuterons are used as projectiles on an enriched calcium-44 target for 3 scenarios: the production of Sc-44g for conventional PET imaging, its production for the new 3 γ imaging technique developed at the SUBATECH laboratory and the production of Sc-44m to be used as Sc-44m/Sc-44g in vivo generator for antibody labelling.
Materials/methods: Experimental production cross section have been measured up to 34 MeV for the Ca-44(d,2n)Sc-44m,Sc-44g reactions, using the stacked-foil technique [1] and gamma-spectrometry, at the ARRONAX cyclotron [2]. The stacks were made of $Ca\text{-}44CO_3$ as targets and aluminum foils as degraders. Monitor foils were made of natural titanium in order to use the IAEA recommended cross section of the Ti-nat(d,x)V-48 reaction. Some results on the production of K-42,43 and Sc-43 have also been obtained but not in all the targets as the main objective was first to properly measure the activity of Sc-44m and Sc-44g. The results are compared with the TALYS code [3] version 1.6. Based on these experimental data, the Thick-Target production Yields (TTY) of Sc-44m and Sc-44g are calculated and compared with those for the proton route for the 3 scenarios [4].
Results: Experimental cross section values have been obtained for the first time for Ca-44(d,2n)Sc-44m,Sc-44g reactions with some information on Sc-43 and K-42,43 also produced during the irradiation. The TALYS results are close to the experimental values for the Ca-44(p,n) and Ca-44(d,2n) reactions whereas it is not able to reproduce the data for the production of potassium isotopes. Our new experimental results have shown that the Sc-44m/Sc-44g cross section and TTY ratios are higher with deuterons than with protons, whatever the incident beam energy.
Conclusions: This study shows that the use of a proton beam is the best choice, as compared to deuterons, to produce Sc-44g for PET imaging using peptides or small molecules with rapid distribution in the body. For the 3 γ imaging technique, Sc-44g has to be produced with protons of 15 MeV to limit the background generated by Sc-44m and Sc-43 decay. The production of the Sc-44m to be used as Sc-44m/Sc-44g in vivo generator for antibody labelling required the highest Sc-44m production rate, with a limited amount of Sc-44g directly produced. The production of Sc-44m is advantageous with deuterons as projectiles, using a calcium-44 carbonate target. Sc-44m can be produced with a 15 MeV deuteron. A higher amount of Sc-44m is produced with a 30 MeV deuteron beam and some cooling time, before the extraction and separation processes, allows to significantly reduce the contribution of directly produced Sc-44g and Sc-43.

Keywords: Sc-44g for PET, 3γ imaging, Sc-44m/Sc-44g in vivo generator

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