**MIRD Calculations:**

The MIRD Committee has defined the mean absorbed dose (D̅) to an organ as the integral of the dose rate (Ḋ) over time (t) (Eq.1), where the dose rate equals the accumulated activity (A) multiplied by the absorbed dose in the target tissue (T) per unit of activity in the source tissue (S), denoted as DF (T🡨S) [[1-5](#_ENREF_1)] (Eq.2). The following calculations describe dosimetry for a subcutaneous tumor after intravenous injection of 177Lu-LCP, which has a mean energy from beta particles, conversion electrons, and Auger electrons of 147 keV [[5](#_ENREF_5)]. For this analysis, the absorbed dose from gamma photons released by 177Lu was not considered.

Strictly speaking, 177Lu present at the edge of the tumor will impart a portion of its energy into the surrounding tissue, and off-target 177Lu present in the surrounding tissue and very close to the tumor will impart a portion of its energy into the tumor. In this approximation, it is assumed that all energy released by the delivered 177Lu is absorbed by the tumor, and no energy from off-target 177Lu is absorbed by the tumor. These calculations quantify the average absorbed dose to the entire tumor according to the equations below:

where:

The tumor studied for these calculations was a subcutaneously inoculated UMUC3/3T3 tumor that was measured to weigh **0.13 grams** and contain **1.63 μCi** of activity from 177Lu when it was dissected from a mouse at t = 24 h after injection of 177Lu-LCP. Taking radioactive decay into account (177Lut1/2 = 6.71 days = 579,744s), this activity corresponds to an activity of **1.81** **μCi** at t = 0 h according to Eq 3. Later, this value will be further adjusted to reflect tumor accumulation of 177Lu-LCP over time.

(3) , where

To convert μCi to Gy/s absorbed by the tumor at t = 0, before taking into account the kinetics of tumor accumulation, the following unit conversions were applied:

This conversions yields the following values at t = 0 for, A, and :

(units of J/s used in Eq 4 and converted to Gy/s)

The dose rate in the tumor may change over time for many reasons. Two of these reasons were accounted for in these calculations:

1. Tumor dose rate will decrease over time due to radioactive decay. Activity at time t can be calculated according to Eq 3. The dose to this tumor with respect to decay at time t is therefore:

(4)

1. The tumor accumulation and pharmacokinetics of systemically injected 177Lu-LCP affect dose rate because at early times after injection, much of the activity is still in circulation. Just after injection, the tumor begins accumulating nanoparticles and therefore activity. By measuring 177Lu-LCP circulation pharmacokinetics in n = 5 mice, the percentage of injected nanoparticles still in circulation as a function of time was determined. In order to estimate the amount of activity within the tumor at 0 < t < 24 h, it was assumed that the tumor accumulation was proportional to the fraction of the injected dose that had left circulation at that time, with the maximum tumor accumulation occurring at t = 24h (Table S1 and Figure S1). For example, at t = 4 h, the pharmacokinetic experiment showed that an average of 87% of 177Lu-LCP had been cleared from circulation, so it was approximated that the tumor in question contained 87% of the activity present at 24 h (the time at which the tumor was dissected). Because 177Lu is a trivalent cation, it tends to remain in the initial organ of deposition, suggesting that this method to approximate the time dependent accumulation of activity is appropriate.



Table S1: 177Lu-LCP Pharmacokinetics**. The fraction of 177Lu-LCP that has left circulation at each time point is tabulated.**



Figure S1: 177Lu-LCP Pharmacokinetics**. Graphical representation of 177Lu PK shown in Table S1. The fast distribution phase is modeled by a linear equation (Eq 5) and the slower elimination phase is modeled by a logarithmic equation (Eq 6).**

Two equations were then calculated to model the two distinct phases of 177Lu-LCP PK:

(5) For 0 < t < 1,800s,

(6) For 1,801 < t < 86,400s,

By applying 177Lu-LCP PK to the radioactive decay equation, one overall dose rate curve was generated (Figure S2). Two separate equations were used to describe the dose rate:

(7) For 0 < t < 1,800s,

(8) For 1,801 < t < 86,400s, a high order polynomial was used to best model the curve:

Solving Eq.1 using this piecewise function therefore yields the following value for total absorbed dose over the first 24h after 177Lu-LCP intravenous injection:



Figure S2: Overall dose rate for 177Lu-LCP**. Graphical representation of overall dose rate. To achieve the best fit, two trend lines were generated. The initial linear equation modeled dose from 0 < t < 1,800s, and a high order polynomial modeled 1,800 < t < 86,400s with an R2 value of 0.999.**



**Figure S3: Fraction of Volume Populated by Cell Nuclei: A) 10x magnification image of DAPI-stained nuclei in an area in section 171; B) Binary representation of nuclear distribution used to quantify nuclear density. Cell nuclei populated ~40% of the total image area. Nuclear radius measured to be an average of ~5 μm.**

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