

Peer Review File

Article Information: <https://dx.doi.org/10.21037/acr-22-6>

Reviewer A

This paper reports on two cases in which calypso soft tissue transponders migrated to the lungs immediately after implantation in the liver. The reported case of this paper will be important for the understanding of calypso soft tissue transponders using radiotherapy with hepatocellular carcinoma.

Major Comment

The author states that the biopsy was performed under CT fluoroscopy in patient B. A)The author should state the distance from the vein. B)In addition, the author states that the distance between the calypso soft tissue transponders and the vein is 1 cm. If this is due to the structure of the calypso, please state so. C)The description of the structure on L149-L152 does not lead to "1 cm".

Reply:

A) Distance was 1-1.5cm from branch right hepatic vein

B) 1 CM is recommended due to the structure of the Calypso beacon. The one CM distance is an arbitrary estimate that is fractionally larger than the maximum length of the soft tissue beacon.

C) Structure described in lines 149-152 is not the Calypso that was inserted. It is the recommended alternative to be evaluated. We now realize it is confusing and we have changed the order of sentences in the last paragraph in discussion.

Change in the text:

A) Added to "Patient B" section;

The migrated posterior Calypso beacon, which was inserted 1-1.5 cm from a branch right hepatic vein, was identified in the right lung (Figure 3C).

B) Last paragraph in discussion has been edited as follows:

We recommend maintaining a safe distance from any branch hepatic vein to the planned location of the beacon. It is not clear how far exactly, but a minimum of one centimeter is probably a safe distance which is fractionally larger than the maximum length of the soft tissue beacon (8.7 mm). Moreover, if the planned insertion site is close to a vessel (as assessed in the pre-insertion infused CT scan or better by an US Doppler), we suggest implanting Calypso beacons under US-guidance after Doppler assessment. Through the Doppler examination, the blood flow can be detected and insertion could be planned to be safely away from the vessels and thus reduce the risk of migration. Alternatively, real time image-fusion technology such as "Volume Navigation" could be considered for accurate placement of calypso beacons under Ultrasound-guidance (12). Finally, while anchored Calypso beacons (Figure 1B) are approved for insertion

in lung (9), one might study the possibility of inserting them in liver as well. Those beacons measure 2 mm in diameter and 8 mm in length (14mm including the anchoring legs). In order to prevent the beacon from migrating within the airways, the beacon has an affixed five-legged anchoring system that expands to 5mm in diameter once deployed. This mechanism could potentially be very useful for better anchoring in liver.

C) Last paragraph in discussion has been edited as detailed above.

Specific Comments

1. L49;Is it necessary to mention SBRT, which stands for Stereotactic body radiation therapy?

Reply;

Agree and we added the abbreviation since it was mentioned again in the abstract (line 52)

Change in the text;

Please see Line 52

2. There are many different names for calypso (Calypso beacons, calypso soft tissue fiducial markers, Calypso fiducials, Calypso soft tissue beacons, Calypso markers, etc.), so please be consistent.

Reply;

Agree it is confusing. We have adjusted the manuscript to use “Calypso soft tissue transponders” or “Calypso beacons”

Change in the text;

Manuscript has been adjusted to use “Calypso soft tissue transponders” or “Calypso beacons”

3. L 148-L149;Remove line breaks.

Reply;

We agree

Change in the text;

We have removed the line break

Reviewer B

Thank you for submitting these interesting cases. Given the paucity of evidence in this space and the multiple options of fiducial markers used in liver SABR, sharing your institutional experience using this device is helpful to guide the choice of fiducial markers for clinicians.

Reviewer C

L107 Where did you plan to place the two Calypso beacons?

Reply;

Corrected, thank you.

Change in the text;

We have added “superior and inferior to the lesion”

L109 Please write which hepatic vein it was.

Reply;

Corrected

Change to the text;

We have added “Branch middle hepatic vein”

L152 Calypso beacons were inserted under CT guidance in patient B. you should describe the suggestions to be taken when using CT to place the Calypso beacon.

Reply;

We agree.

Change to the text;

Please see the edited last paragraph in discussion as mentioned above under “Reviewer A, Major comments, B”.

L154 It is easy to perform US Doppler. Therefore, US Doppler should be performed in all patients, regardless of the distance of the hepatic vein where the Calypso beacon is placed, in order to perform it safely.

Reply;

We believe that CT with IV contrast prior to insertion can guide best location for insertion. However, in case of any doubt, US Doppler will be preferred.

Change to the text;

Please see the edited last paragraph in discussion as mentioned above under “Reviewer A, Major comments, B”.

L154 I think real-time image fusion technology in ultrasonography is a good method to reduce the risk, why don't you also mention about it? (doi: 10.1177/0284185120934479. Epub 2020 Jun 26.)

Reply;

We accept this very useful suggestion.

Change to the text;

Please see the edited last paragraph in discussion as mentioned above under “Reviewer A, Major comments, B”.