OPEN PEER REVIEW

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Iranian Journal of Radiology
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Published in: Iranian Journal of Radiology: 18(2); e113389

Peer Review Report for "Computed Tomography-Guided Cryoablation for Adrenal Metastasis Secondary to Non-small-cell Lung Cancer"

Author(s): Jie-Fei Cheng, Wen Xu, Pei-Pei Liu

Review Timeline:

Submit Date: 30 Jan 2021
Revised Date: 8 May 2021
Accepted Date: 15 May 2021

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

mohammad momeni: Reviewer | **Revision** (0) 12 Feb 2021

Dear AE,
I read with interest the manuscript, this research is very valuable clinically. However, the authors may consider the following suggestions to improve their work:
- In the material and method section, Please mentioned what was your plan for anticipated problems such as hypertension crisis during the procedure, as we see blood pressure increases were observed in 7 out of 34.
- Please explain the fig 1b in detail and add some markers and arrows as students and non-interventionist might not be familiar with these procedures.
Thanks.

Shahram Akhlaghpour: Reviewer | **Revision** (0) 12 Feb 2021

Dear AE,
The article describes 34 NSCLC patients with adrenal metastases who were treated by the cryoablation technique. The topic is interesting and has new data.
The English writing needs improvement.
The reason that authors decide to find the role and efficacy of Cryoablation of specific adrenal metastasis (here NSCLC) is not well described and needs more explanation in the

introduction.
There is no data about the patient sedation(local or general anesthesia)
There is data about the average size of adrenal metastases in the table (almost 2.8 to 3 cm); however, no data regarding the number of Cryoprobe inserted.
The Adrenal metastases size in this stud is < 3 cm. We know it is a major criterion in ablation success, So it is a critical point when comparing the result with other studies to mention their adrenal metastases size.
The authors mentioned that They use 10 min freeze cycle and 3 min thawing cycle. However, they didn't note that if after CT control, the Ice Ball was not reasonable what they did?
Thanks.

REFEREE: Reviewer | **Revision** (0) 13 Feb 2021

Dear AE,
Although, the authors of the current manuscript try to do a high-quality study; but according to the methodology view, it must be said that it has three major concerns: small sample size, inappropriate design based on study objective, and lack of control group that received another treatment.
1. Sample size: In tables 1 and 2, the data were analyzed in terms of two groups of lung cancer patients separately, including Squamous cell carcinoma (16) and Adenocarcinoma (18). This division of samples negatively affects on study's statistical power.
2. The study objective mentioned that "To assess the clinical efficacy of CT-guided cryoablation for treating AM secondary to NSCLC." It can be assessed efficacy and effectiveness of a treatment in the experimental and clinical trial study, respectively; but here, it used of retrospective cohort design.
3. Lack of control group: For evaluation of treatment it must be used a control group that received another intervention; otherwise, conclusions and analysis about the effectiveness of treatment become impossible.
Thanks.

REFEREE: Associate Editor | **Revision** (0) 14 Feb 2021

Dear EIC,
The manuscript is studied, and there are some comments which should be addressed by the author. According to the comments, the document needs major revision.
Kind regards,

REFEREE: EIC | **Revision** (0) 15 Feb 2021

Dear authors,
Your article needs Major Revision.
Regards

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear Prof. Kavous Firouznia:

Thank you for your kind letter of **Iran J Radiol | ID: 113389, rev [0] | Manuscript Needs Major Revision**. We revised the manuscript in accordance with the reviewers' comments, and carefully proof-read the manuscript to minimize the typographical, grammatical and bibliographical errors.

Reviewers' Comments:

Reviewer 1:

The article describes 34 NSCLC patients with adrenal metastases who were treated by the cryoablation technique. The topic is interesting and has new data.

1. The English writing needs improvement.

Answer: We found a native speaker to revise it.

2. The reason that authors decide to find the role and efficacy of Cryoablation of specific adrenal metastasis (here NSCLC) is not well described and needs more explanation in the introduction.

Answer: We added some contents.

3. There is no data about the patient sedation(local or general anesthesia).

Answer: All patients were treated under the local anesthesia. We added it.

4. There is data about the average size of adrenal metastases in the table (almost 2.8 to 3 cm); however, no data regarding the number of Cryoprobe inserted.

Answer: We added it.

The Adrenal metastases size in this study is < 3 cm. We know it is a major criterion in

ablation success, So it is a critical point when comparing the result with other studies to mention their adrenal metastases size.

Answer: We added them.

The authors mentioned that They use 10 min freeze cycle and 3 min thawing cycle. However, they didn't note that if after CT control, the Ice Ball was not reasonable what they did?

Answer: The ice ball is the dimension of the frozen area after CT-guided cryoablation. It is only used for evaluating the instant effectiveness of CT-guided cryoablation. Therefore, the ice ball cannot be used for the long-term follow-up.

Reviewer 2:

I read with interest the manuscript, this research is very valuable clinically. However, the authors may consider the following suggestions to improve their work:

-In the material and method section, Please mentioned what was your plan for anticipated problems such as hypertension crisis during the procedure, as we see blood pressure increases were observed in 7 out of 34.

Answer: We added it.

-Please explain the fig 1b in detail and add some markers and arrows as students and non-interventionist might not be familiar with these procedures.

Answer: We added them.

Reviewer 3:

Although, the authors of current manuscript try to do a high quality study; but according to methodology view, it must be said that it has three major concerns: small sample size, inappropriate design based on study objective, and lack of control group that received another

treatment.

1. Sample size: In tables 1 and 2, the data analyzed in terms of two groups of lung cancer patients separately, including Squamous cell carcinoma (16) and Adenocarcinoma (18). This division of samples negatively effects on study statistical power.

Answer: The limited sample size did decrease the statistical power. Further multicenter, large sample studies are still required.

2. The study objective mentioned that "To assess the clinical efficacy of CT-guided cryoablation for treating AM secondary to NSCLC." It can be assessed efficacy and effectiveness of a treatment in experimental and clinical trial study, respectively; but here, it used of retrospective cohort design.

Answer: This is a retrospective study. Many previous studies regarding CT-guided ablation for AM are all retrospective studies [1-3].

1. Hasegawa T, Yamakado K, Nakatsuka A, et al. Unresectable adrenal metastases: clinical outcomes of radiofrequency ablation. Radiology. 2015;277(2):584-593. doi: 10.1148/radiol.2015142029.

2. Frenk NE, Daye D, Tuncali K, et al. Local control and survival after image-guided percutaneous ablation of adrenal metastases. J Vasc Interv Radiol. 2018;29(2):276-284. doi: 10.1016/j.jvir.2017.07.026.

3. Zhang W, Sun LJ, Xu J, et al. Computed tomography-guided cryoablation for adrenal metastases: local control and survival. Medicine (Baltimore). 2018;97(51):e13885. doi: 10.1097/MD.0000000000013885.

3. Lack of control group: For evaluation of a treatment it must be used a control group that

received another intervention; otherwise, conclusions and analysis about the effectiveness of treatment become impossible.

Answer: Lack of control group is a limitation of this study. Many previous studies regarding CT-guided ablation for AM also have a single group [1-3]. Although we have no cases who were treated by other method, we compared the data between patients with squamous cell carcinoma and adenocarcinoma and made a conclusion that patients with AM secondary to SCC may benefit the most to cryoablation.

1. Hasegawa T, Yamakado K, Nakatsuka A, et al. Unresectable adrenal metastases: clinical outcomes of radiofrequency ablation. Radiology. 2015;277(2):584-593. doi: 10.1148/radiol.2015142029.

2. Frenk NE, Daye D, Tuncali K, et al. Local control and survival after image-guided percutaneous ablation of adrenal metastases. J Vasc Interv Radiol. 2018;29(2):276-284. doi: 10.1016/j.jvir.2017.07.026.

3. Zhang W, Sun LJ, Xu J, et al. Computed tomography-guided cryoablation for adrenal metastases: local control and survival. Medicine (Baltimore). 2018;97(51):e13885. doi: 10.1097/MD.0000000000013885.

Associate Editor's Comments:

Associate Editor 1:

Dear Dr. Pei-Pei Liu

Thank you again for submitting your manuscript to "Iranian Journal of Radiology" for peer review. It has now completed our peer-review process and I write to inform you that we

would like you to revise your manuscript.

The comments on your paper are appended to the bottom of this letter, along with a list of suggested amendments. We would like you to revise your manuscript taking regard of these comments. If you are prepared to undertake the revision work required to satisfy these concerns with your manuscript, one or more reviewers, as well as myself, will review your revised manuscript.

In revising your work, please indicate your changes and relate them to each concern. We would appreciate receiving your revised manuscript no later than March 10, 2020

Reviewer 1#

Although, the authors of current manuscript try to do a high quality study; but according to methodology view, it must be said that it has three major concerns: small sample size, inappropriate design based on study objective, and lack of control group that received another treatment.

1. Sample size: In tables 1 and 2, the data analyzed in terms of two groups of lung cancer patients separately, including Squamous cell carcinoma (16) and Adenocarcinoma (18). This division of samples negatively effects on study statistical power.

Answer: The limited sample size did decrease the statistical power. Further multicenter, large sample studies are still required.

2. The study objective mentioned that "To assess the clinical efficacy of CT-guided cryoablation for treating AM secondary to NSCLC." It can be assessed efficacy and effectiveness of a treatment in experimental and clinical trial study, respectively; but here, it used of retrospective cohort design.

Answer: This is a retrospective study. Many previous studies regarding CT-guided ablation for AM are all retrospective studies [1-3].

1. Hasegawa T, Yamakado K, Nakatsuka A, et al. Unresectable adrenal metastases: clinical outcomes of radiofrequency ablation. Radiology. 2015;277(2):584-593. doi: 10.1148/radiol.2015142029.

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3. Lack of control group: For evaluation of a treatment it must be used a control group that received another intervention; otherwise, conclusions and analysis about the effectiveness of treatment become impossible.

Answer: Lack of control group is a limitation of this study. Many previous studies regarding CT-guided ablation for AM also have a single group [1-3]. Although we have no cases who were treated by other method, we compared the data between patients with squamous cell carcinoma and adenocarcinoma and made a conclusion that patients with AM secondary to SCC may benefit the most to cryoablation.

1. Hasegawa T, Yamakado K, Nakatsuka A, et al. Unresectable adrenal metastases: clinical outcomes of radiofrequency ablation. Radiology. 2015;277(2):584-593. doi: 10.1148/radiol.2015142029.

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3. Zhang W, Sun LJ, Xu J, et al. Computed tomography-guided cryoablation for adrenal metastases: local control and survival. Medicine (Baltimore). 2018;97(51):e13885. doi: 10.1097/MD.0000000000013885.

Reviewer 2#

The article describes 34 NSCLC patients with adrenal metastases who were treated by the cryoablation technique. The topic is interesting and has new data.

1. The English writing needs improvement.

Answer: We found a native speaker to revise it.

2. The reason that authors decide to find the role and efficacy of Cryoablation of specific adrenal metastasis (here NSCLC) is not well described and needs more explanation in the introduction.

Answer: We added some contents.

3. There is no data about the patient sedation(local or general anesthesia).

Answer: All patients were treated under the local anesthesia. We added it.

4. There is data about the average size of adrenal metastases in the table (almost 2.8 to 3 cm); however, no data regarding the number of Cryoprobe inserted.

Answer: We added it.

The Adrenal metastases size in this study is < 3 cm. We know it is a major criterion in

ablation success, So it is a critical point when comparing the result with other studies to mention their adrenal metastases size.

Answer: We added them.

The authors mentioned that They use 10 min freeze cycle and 3 min thawing cycle. However, they didn't note that if after CT control, the Ice Ball was not reasonable what they did?

Answer: The ice ball is the dimension of the frozen area after CT-guided cryoablation. It is only used for evaluating the instant effectiveness of CT-guided cryoablation. Therefore, the ice ball cannot be used for the long-term follow-up.

Reviewer 3#

I read with interest the manuscript, this research is very valuable clinically. However, the authors may consider the following suggestions to improve their work:

-In the material and method section, Please mentioned what was your plan for anticipated problems such as hypertension crisis during the procedure, as we see blood pressure increases were observed in 7 out of 34.

Answer: We added it.

-Please explain the fig 1b in detail and add some markers and arrows as students and non-interventionist might not be familiar with these procedures.

Answer: We added them.

OPEN PEER REVIEW

Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (1) 2 Mar 2021

Dear AE,
While thanking the authors for providing answers to the questions, despite the clinical value of this study, it should be said that from the methodological point of view, the study design is not appropriate to its purpose. Unfortunately, a retrospective study can not comment on the effectiveness of treatment.
Thanks.

REFEREE: Associate Editor | **Revision** (1) 11 Mar 2021

Dear EIC,
It is our pleasure to inform the authors that the mentioned article has been accepted for publication in the journal.
Best regards

Madjid Shakiba: Associate Editor | **Revision** (1) 28 Mar 2021

Dear EIC,
Comments for the authors:
1-the authors mentioned: “Local recurrence was defined by the presence of new tumor enhancement within the ablated region” it is unclear if what is the time of this event? In the first follow up?
2-the authors mentioned: “Local RFS was defined as the time between treatment and AM recurrence, death, or most recent follow-up” there are two considerations in this definition:
I-It seems death should not be considered as the criteria for RFS as the patients that are died because of metastasis have experience recurrence many times before the death and death could not be considered as the criteria for RFS. In fact, time of death is appropriate for overall survival, not for RFS.
II-In addition, what is the meaning of most recent follow-up in this definition? It is probable that the patient has no recurrence in the most recent follow-up, so he/she should be considered as event negative in survival analysis. If patient is negative for AM in most recent follow up, he/she should be considered as event positive.
3-the authors defined: “OS was the time from treatment to death or most recent follow-up” same as the previous question, if the patient is alive in the most recent follow-up, he/she should be considered event negative.

4-the authors mentioned: “Systematic RFS was defined as the time between treatment and AM recurrence, extra-adrenal recurrence, death, or most recent follow-up.” Similar to question 2, I think in this definition, the authors should mention “Systematic RFS was defined as the time between treatment and extra-adrenal recurrence.” Please clarify.
5-the authors mentioned: “There were 6 and 7 patients in SCC and adenocarcinoma groups who underwent chemotherapy after cryoablation, respectively” what was the criteria for chemotherapy which patients underwent chemotherapy?
6-what is the criteria for Moderate blood pressure increases?
7-the authors mentioned: “No patient suffered from the hypertensive crisis including hematoma, hemorrhage, and damage to the surrounding tissues following cryoablation.” Do “hematoma, hemorrhage, and damage to the surrounding tissues” happen after hypertensive crisis? Are these complications related to hypertensive crisis?
8-what was the follow-up time of patients? [mean and median] was the follow-up time different for SCC and adenocarcinoma? it is useful to know how many time the patients that did not experience recurrence were followed up. In fact, I suppose the 22 months [median] for local RFS is the median time of RFS in 8 patients who experienced local recurrence [5 and 3 patients in SCC and adenocarcinoma] not for other patients. Please explain.
9-the authors mentioned: ‘The 1-, 3-, and 5-year local RFS rates were 100% and 77.8%, 56.2% and 16.9%, and 15.8% and 0%, in SCC and adenocarcinoma groups, respectively.’ This sentence is unclear; it seems better to write as: “1-, 3-, and 5-year local recurrence rate were 0, 22.2% and 43.8%, respectively for SCC and …… for adenocarcinoma respectively…..” [I mean it is better to be written based on the rate of recurrence in each time session]. In addition, it is questionable what is the meaning of 16.9%, 15.8% and 0% for adenocarcinoma? Are these numbers correct? They are so different from the numerical profile of SCC. Please evaluate and correct if it is needed.
10-in the “Systematic RFS” section, the authors mentioned: “The median time for systematic recurrence was 15 months.” While they mentioned later in this part: “The median systematic RFS for all patients was 22 months” are these two parts consistent with each other? They seem to be different numbers for a single variable and so, it seems to be wrong.
11-the authors mentioned: “The 1-, 3-, and 5-year systematic RFS rates were 93.8% and 72.2%, 50.0% and 7.4%, and 11.9% and 0%, in SCC and adenocarcinoma groups, respectively” I propose a similar question for this part as the my question 8. Please correct same as the previous question.
12-what was the statistical test for comparing survivals in SCC and adenocarcinoma groups? [log rank test?] please add in paper.
13-the authors mentioned: “The 1-, 3-, and 5-year OS rates were 100% and 88.9%, 68.8% and 16.3%, and 45.1% and 16.3%, in SCC and adenocarcinoma groups, respectively.” I propose the same question as question 8 for this part too.
14-what were the variables in cox regression analysis? For example, did the authors consider size of tumor, gender, Previous chemotherapy, and primary complete ablation rate in cox analysis?
15-it is better the authors add standard deviation to values of table 1 and 2.
Thanks.

REFEREE: EIC | **Revision (1)** 30 Mar 2021

Dear authors,

Your article needs Major Revision.

Regards

OPEN PEER REVIEW

Revision (2)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear Prof. Kavous Firouznia:

Thank you for your kind letter of **Iran J Radiol | ID: 113389, rev [1] | Manuscript Needs Major Revision**. We revised the manuscript in accordance with the reviewers' comments, and carefully proof-read the manuscript to minimize the typographical, grammatical and bibliographical errors.

Associate Editor's Comments:

1-the authors mentioned: "Local recurrence was defined by the presence of new tumor enhancement within the ablated region" it is unclear if what is the time of this event? In the first follow up?

Answer: The time of this event is in the first follow-up. However, if a patient was found with local recurrence, the follow-up was still continued until death or the point of December 2020.

2-the authors mentioned: "Local RFS was defined as the time between treatment and AM recurrence, death, or most recent follow-up" there are two considerations in this definition:

I-It seems death should not be considered as the criteria for RFS as the patients that are died because of metastasis have experience recurrence many times before the death and death could not be considered as the criteria for RFS. In fact, time of death is appropriate for overall survival, not for RFS.

II-In addition, what is the meaning of most recent follow-up in this definition? It is probable that the patient has not recurrence in the most recent follow up, so he/she should be considered as event negative in survival analysis. If patient is negative for AM in most recent follow up, he/she should be considered as event positive.

Answer: If a patient has experienced recurrence many times before the death, the RFS was calculated from the treatment to the first recurrence. If a patient died without local recurrence, we agree the reviewer's suggestion, it should be considered as an event negative. The most recent follow-up should be revised as the last follow-up. If a patient has not recurrence in follow up, he/she should be considered as event negative. We agree the reviewer's suggestion. We also revised the results about the Local RFS.

3-the authors defined: "OS was the time from treatment to death or most recent follow-up" same as previous question, if patient is alive in the most recent follow up, he/she should be considered event negative.

Answer: We agree it.

4-the authors mentioned: "Systematic RFS was defined as the time between treatment and AM recurrence, extra-adrenal recurrence, death, or most recent follow-up." Similar to question 2, I think in this definition, the authors should mention "Systematic RFS was defined as the time between treatment and extra-adrenal recurrence." Please clarify.

Answer: We revised it.

5-the authors mentioned: "There were 6 and 7 patients in SCC and adenocarcinoma groups who underwent chemotherapy after cryoablation, respectively" what was the criteria for chemotherapy which patients underwent chemotherapy?

Answer: All patients could undergo chemotherapy after cryoablation. However, only 6 and 7 patients in SCC and adenocarcinoma groups underwent chemotherapy after cryoablation in this study. For the remaining patients who did not undergo chemotherapy, some patients did not receive chemotherapy because their economic condition was not well, while some

patients refused to receive chemotherapy after cryoablation. Definitely, this is a limitation of this study.

6-what is the criteria for Moderate blood pressure increases?

Answer: There is no strict criteria about it. These patients experienced increased systolic or diastolic blood pressure < 10 mmHg.

7-the authors mentioned: “No patient suffered from the hypertensive crisis including hematoma, hemorrhage, and damage to the surrounding tissues following cryoablation.” Do “hematoma, hemorrhage, and damage to the surrounding tissues” happen after hypertensive crisis? Are these complications related to hypertensive crisis?

Answer: Thanks for your comment. We find that the description is not right. The complications (hematoma, hemorrhage, and damage to the surrounding tissues) are not related to hypertensive crisis. W revised it.

8-what was the follow up time of patients? [mean and median] was the follow up time different for SCC and adenocarcinoma? it is useful to know how many time the patients that did not experience recurrence were followed up. In fact, I suppose the 22 months [median] for local RFS is the median time of RFS in 8 patients experienced local recurrence [5 and 3 patients in SCC and adenocarcinoma] not for other patients. Please explain.

Answer: We added the follow-up time. The mean follow-up was significantly higher in SCC group than that in the adenocarcinoma group (35.9 ± 14.9 vs. 22.6 ± 14.4 months; P = 0.013) because the OS was significantly higher in the SCC group compared with the adenocarcinoma group. All patients were followed up until to death or the point of December 2020. No patient was lost in follow-up. Previously, we calculated the median local RFS was

22 months for all patients. However, as the reviewer mentioned above, the patients who did not experience local recurrence should be considered as event negative. Therefore, we re-calculated the median local RFS again and the median local RFS was 51 months for all patients.

9-the authors mentioned: ‘The 1-, 3-, and 5-year local RFS rates were 100% and 77.8%, 56.2% and 16.9%, and 15.8% and 0%, in SCC and adenocarcinoma groups, respectively.’ This sentence is unclear; it seems better to write as: “1-, 3-, and 5-year local recurrence rate were 0, 22.2% and 43.8%, respectively for SCC and …… for adenocarcinoma respectively…..” [I mean it is better to be written based on the rate of recurrence in each time session]. In addition, it is questionable what is the meaning of 16.9%, 15.8% and 0% for adenocarcinoma? Are these numbers correct? They are so different from the numerical profile of SCC. Please evaluate and correct if it is needed.

Answer: As the reviewer mentioned above, the patients who did not experience local recurrence should be considered as event negative. Therefore, we re-calculated these rates again. We also used the 1-, 3-, and 5-year local recurrence rates according to the reviewer’s suggestion.

10-in the “Systematic RFS” section, the authors mentioned: “The median time for systematic recurrence was 15 months.” While they mentioned later in this part: “The median systematic RFS for all patients was 22 months” are these two parts consistent with each others? They seems to be different numbers for a single variable and so, it seems to be wrong.

Answer: The 15 months was only for the 5 patients who experienced extra-adrenal recurrence. The median time from treatment to systematic recurrence was 15 months for

these 5 patients who experienced extra-adrenal recurrence. We revised it. As the reviewer mentioned above, the patients who did not experience extra-adrenal recurrence should be considered as event negative. Therefore, we re-calculated the median systematic RFS again and the median systematic RFS was 56 months for all patients.

11-the authors mentioned: “The 1-, 3-, and 5-year systematic RFS rates were 93.8% and 72.2%, 50.0% and 7.4%, and 11.9% and 0%, in SCC and adenocarcinoma groups, respectively” I propose a similar question for this part as the my question 8. Please correct same as the previous question.

Answer: We revised it.

12-what was the statistical test for comparing survivals in SCC and adenocarcinoma groups? [log rank test?] please add in paper.

Answer: We added it.

13-the authors mentioned: “The 1-, 3-, and 5-year OS rates were 100% and 88.9%, 68.8% and 16.3%, and 45.1% and 16.3%, in SCC and adenocarcinoma groups, respectively.” I propose the same question as question 8 for this part too.

Answer: We revised it.

14-what were the variables in cox regression analysis? For example, did the authors consider size of tumor, gender, Previous chemotherapy, and primary complete ablation rate in cox analysis?

Answer: The variables in table 3 are the variables with $P < 0.1$ on univariate Cox regression analysis. Size of tumor, gender, Previous chemotherapy, and primary complete ablation rate are not significant ($P > 0.1$) on univariate Cox regression analysis. We added these variables

in table 3.

15-it is better the authors add standard deviation to values of table 1 and 2.

Answer: We added them. In table 2, the survival time is presented with the median value, therefore, standard deviation is not needed.

OPEN PEER REVIEW

Revision (2)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Madjid Shakiba: Associate Editor | **Revision** (2) — 4 May 2021

Dear EIC,
The authors have revised many points. The only thing is that logically, OS [in terms of median months] should be longer than the local and systemic RFS,; while in table 2, OS is 22 months in Adenocarcinoma. Group while the local and systemic RFS are 56 and 49 months. Please explain and correct. [this profile is correct for SCC].
Thanks.

REFEREE: EIC | **Revision** (2) — 5 May 2021

Dear authors,
Your article needs Minor Revision.
Regards

OPEN PEER REVIEW

Revision (3)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear Prof. Kavous Firouznia:

Thank you for your kind letter of Iran J Radiol, manuscript ID: 113389, rev [2], needs Minor Revision. We revised the manuscript in accordance with the reviewers' comments, and carefully proof-read the manuscript to minimize the typographical, grammatical and bibliographical errors.

Associate Editor's Comments:

Associate Editor 1:

The authors have revised many points. The only thing is that logically, OS [in terms of median months] should be longer than the local and systemic RFS,; while in table 2, OS is 22 months in Adenocarcinoma. Group while the local and systemic RFS are 56 and 49 months. Please explain and correct. [this profile is correct for SCC]

Answer: When we calculated the local and systemic RFS, the patients died without local or systemic recurrence were classified as censored data. Therefore, the OS was shorter than the local and systemic RFS owing to the loss of censored data. We have re-calculated and corrected the local and systemic RFS.

OPEN PEER REVIEW

Revision (3)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Associate Editor | **Revision** (3) 15 May 2021

Dear EIC
Based on the authors' answers to the reviewers' comments, the reviewer(s) have recommended publication.
Kind regards.

REFEREE: EIC | **Revision** (3) 15 May 2021

Dear authors,
Your article is acceptable for the publication in IJR.
Regards