

## **A comparison of skin dose estimation between thermoluminescent dosimeter and treatment planning system in prostatic cancer: A brachytherapy technique**

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A Comparison of Different Thermo-Luminescent Dosimeters for Verification of Treatment  
Planning System Accuracy in Brachytherapy of Prostatic Cancer  
Journal of Clinical and Translational Research

Dear Mr. Abdi Goushbolagh,

Reviewers have now commented on your paper. You will see that they are advising that you  
revise your manuscript. If you are prepared to undertake the work required, I would be  
pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below and attached to this email.

If you decide to revise the work, please submit a list of changes or a rebuttal against each  
point which is being raised when you submit the revised manuscript. Also, please ensure that  
the track changes function is switched on when implementing the revisions. This enables the  
reviewers to rapidly verify all changes made.

Your revision is due by Nov 23, 2020.

To submit a revision, go to <https://www.editorialmanager.com/jctres/> and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: Comments:

- 1) The authors used two TLDs, however it is not explain which TLDs had better performance and results? Please mention it in the text.
- 2) I think the percentage of agreement could be worded differently just as a factual figure and mention of clinical relevance at these dose levels. It is important that note, this agreement is true for the doses used in the current study and may vary for the other doses and even other energies.
- 3) It is helpful to express the current accuracy of TPS and what is the recommended level of accuracy? Quantify it with the appropriate references.
- 4) Kindly write the dimensions of GR-200 as in TLD-100. Also, the dimensions of the holes should be revised in proportion to the dimensions of the TLDs on the phantom.
- 5) There are some grammatical problems, then the authors should revise the whole text by helping English expertise.

Reviewer #2: ABSTRACT

1. Line 13: The full expression for GR should come before the abbreviation GR-200
2. Line 13: Delete 'precisely'
3. Line 14 : Replace 'in' with 'at'
4. Correct Line 14 to read: at 3 different points (anterior, left and right) using five TLDs each.
5. Line 15: Use 'Percentages' instead of 'Percentage';
6. Line 15: 'were' should replace 'was'
7. Line 21: Delete 'Regarding the results; Start with - The accuracy .....
8. Line 8: Replace using with 'in'

INTRODUCTION

1. Line 30: Delete 'of the' immediately following 'among'
2. Line 30: Replace 'common' with 'prevalent'
3. Line 31: The first part of the sentence needs grammatical editing to read: 'Very few people younger than 50 years are diagnosed to have prostate cancer.....

- 4 Line 38: replace 'branches' with 'components'
5. Line 49: replace 'the' with 'a'
6. Line 52: Replace 'more precise' with 'Accurate'
7. Line 52: Replace 'lead to' with 'would result in a'
8. Line 53: Revise the sentence to read: 'Verification of the accuracy of the TPS is therefore important'
9. Line 57: State the references for the statement "Several studies ..... for prostate cancer treatment".
9. Line 58/59: Delete 'while recently' and start the next sentence with 'Considerations for in-vivo dosimetry in 60 Co-based (with a higher photon energy) brachytherapy is also on the increase (cite: Journal of Contemporary Brachytherapy. doi:10.5114/jcb.2015.56767)
10. Line 60: Replace 'set out' with 'was designed'
11. Line 60/61: This study was designed to evaluate the TPS accuracy for 60Co brachytherapy of prostate cancer using two TLD types, TLD-100 and GR-200.

## MATERIALS AND METHODS

1. Line 63: Is 'microselectron' from BEBIG? Please check and use what is appropriate.
2. Line 67: 'cooperated' should be replaced with 'included'
3. Line 67: 'aware of' should be replaced with 'informed of the'
4. Line 68: three or five ?
- 5 Line 69: Replace 'corporation' with 'participation'
6. Line 73/74: Need editing to read "Dose read-out was subsequently carried out using LTM Reader .....
- Line 91: replace 'regarding to' with 'in the'
- Line 100: Is it SagiNova or SagiPlan? Confirm and use the right word.
- Line 106: replace 'in' with 'at the'
- Line 124: Express the meanings of the different parameters contained in Equation 2 and provide the reference.
- Line 164: Table 3 (not table 3)
- Line 164: Delete 'According to this table'
- Line 164- 166: Need a thorough editing for enhanced grammar to read: "The positive values show that the TLD dose measurement were higher than TPS calculated doses and the negative values imply the opposite"
- Line 168: replace 'deference' with 'deviation'
- Line 173 - 174: "The movement of markers .....can be the main reason. " Include a statement to address how this could be avoided.
- Line 175: Replace 'is' with 'was'

Line 176- 177 : " The result would seem .....displacement" is totally confusing and needs a thorough grammatical editing!

The Tables also require some formatting and corrections as follow:

Table 1: Revise its Title to : TPS-Based Calculated Dose (cGy) at three points

The three dose columns should read: Anterior, Left, Right to avoid repeated use of dose and unit

All dose values should be to 1 decimal place e.g 120 to appear as 120.0 etc.

Table 3:

Revise Table's title to read:

Differences (%) between TLD-100 and GR-200 measurements with respect to TPS-calculated doses.

Avoid repeated used of the term 'Patient'. Use the same pattern in Table 1

It is also best to have the percentage differences (at a given point e.g Anterior) for different TLDs next to each other.

That is:

Anterior	
TLD 100	GR-200
1.12	3.84
-1.25	1.62

etc...

Reviewer #3: General Comment:

The title of the study suggests that different TLD dosimeters were tested for their adequacy of independently verifying the accuracy of a Treatment Planning System (TPS) dose estimations. However, the study design uses the TPS dose estimation as the "reference dose" to compare the TLD data against, which is unfortunately not logical.

Two potential alternatives:

- 1) If the study design is only intended to demonstrate the TLD dosimetry as compared to TPS estimations for skin, update relevant language in the title and the conclusions ("...TLD...dosimetry could be an appropriate method for evaluating TPS dose calculation accuracy in <sup>60</sup>Co brachytherapy technique").
- 2) If the study design is intended to demonstrate some of GR-200's adequacy to verify TPS accuracy, the authors may want to consider using TLD-100 as the reference to compare against for both Gr-200 and TPS methods, as long as sufficient justification is provided as to why TLD-100 dosimetry can serve as the reference dosimetry.

Specific Comments:

Line 11: "Entrance skin dose" (ESD) should be replaced by "skin dose" or "exit skin dose" here and throughout the manuscript. For prostate brachytherapy, the radiation is emitted from a source inside the patient body and then reaches the skin, so the use of "entrance" is not accurate.

Line 59: "~1.25 MV" uses an inaccurate unit, MV. The unit should be MeV instead for the gamma emission energies of Co-60.

Line 69: "corporation" should be "cooperation" or "participation".

Lines 81-84: The TLD calibration setup appears to have two potentially significant deviation from the actual measurement setup:

- 1) Angular geometry: the calibration takes place at 100cm distance to the TLDs, i.e. perpendicular irradiation, whereas the actual measurement setup involves much shorter distance in the patient body. Can the authors please address the concern of potential angular response dependency issues with the TLD chips?

- 2) Backscatter: the calibration takes place with 5cm of Perspex phantom for backscattering, whereas the actual measurement setup does not have any backscattering. Can the authors please address the discrepancy in the backscattering environment as well as the adequacy of calibration setup?

Line 105: Please spell out and clarify "EQD2".

Lines 117-119: Please identify small-letter, n. Is it the same as N?

Line 127: the reference #16 appears to be a typo, please provide the correct reference number.

Lines 163-168: Three occurrences of "deference" should be changed to "difference".

Lines 169: What makes the TPS dose the "reference dose"?

Line 210: Invalid Citation.

Table 2: The data presentation is confusing, are the two numbers in each field meant for TLD-100 and GR-200, respectively? If that is the case, listing the values in a new column for GR-200 will be better.

Table 2: Please explain why the uncertainty for Holder correction factors ( $F_{hol}$ ) are different for TLD-100 and Gr-200.

Figure 2: Why are the horizontal axis "Dose (cGy)", is that the un-corrected dosimeter reading? Please clarify in the manuscript and/or the Figure title.

Reviewer #4: I have gone through the manuscript and suggested few modifications and also asked for few clarifications.

There is additional documentation related to this decision letter. To access the file(s), please click the link below. You may also login to the system and click the 'View Attachments' link in the Action column.

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Authors' response

Dear editor-in-chief of "**Journal of Clinical and Translational Research**"

Dr. Michal Heger,

On behalf of my co-authors, we thank you very much for giving us an opportunity to revise our manuscript. We appreciate the positive and constructive comments and suggestions on our manuscript. We have studied comments carefully and made corrections which we hope meet with approval. The details are indicated in the manuscript file named "Manuscript-revised". And our responses to the reviewer's comments are listed below one by one (the answers are shown in Blue color). The reviewers' answers in the text highlighted with yellow color.

Sincerely yours,

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Reviewer 1

1) The authors used two TLDs, however it is not explain which TLDs had better performance and results? Please mention it in the text.

**Answer:** In the new version, we have explained the exact aim, in other words, we did not assume the TPS calculation as reference, and we just compared the results of skin TLD dosimetry and TPS calculations to show that TLD dosimetry can be used as an appropriate quality assurance procedure of TPS dose calculations. Theoretically, TLDs yield more accurate dose in skin compared to TPS calculations. But regarding your comment we brought a sentence in conclusion section, showing which TLD type had lower differences with TPS calculations.

2) I think the percentage of agreement could be worded differently just as a factual figure and mention of clinical relevance at these dose levels. It is important that note, this agreement is true for the doses used in the current study and may vary for the other doses and even other energies.

**Answer:** Your comment is absolutely true. The comparison results could be very different in other cancer sites or brachytherapy techniques. But it must mention that the obtained skin doses were from the patients undergoing prostate brachytherapy, and our aim was to show the skin TLD dosimetry as an appropriate quality assurance procedure for TPS dose calculations in prostate cancer patients undergoing brachytherapy. We rewrite the aim to illustrate the study specific objectives. Thank you.

3) It is helpful to express the current accuracy of TPS and what is the recommended level of accuracy? Quantify it with the appropriate references.

**Answer:** The relevant explanations about the TPS measurement accuracy and also the recommended level were added in the discussion section of the edited manuscript.

4) Kindly write the dimensions of GR-200 as in TLD-100. Also, the dimensions of the holes should be revised in proportion to the dimensions of the TLDs on the phantom.

**Answer: Thanks for your comment. The TLD dimensions were written in the edited version.**

**The dimension of the holes in the calibration phantom were relatively similar to TLD dimensions ( $3.2 \times 3.2 \text{ mm}^2$ ), except the depth, which is 2 millimeter in the phantom and TLD thickness are about 1 millimeter.**

5) There are some grammatical problems, then the authors should revise the whole text by helping English expertise.

**Answer: The whole text of the manuscript was revised by an English expert.**

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Reviewer 3

General Comment:

The title of the study suggests that different TLD dosimeters were tested for their adequacy of independently verifying the accuracy of a Treatment Planning System (TPS) dose estimations. However, the study design uses the TPS dose estimation as the "reference dose" to compare the TLD data against, which is unfortunately not logical.

Two potential alternatives:

1) If the study design is only intended to demonstrate the TLD dosimetry as compared to TPS estimations for skin, update relevant language in the title and the conclusions ("...TLD...dosimetry could be an appropriate method for evaluating TPS dose calculation accuracy in  $^{60}\text{Co}$  brachytherapy technique").

2) If the study design is intended to demonstrate some of GR-200's adequacy to verify TPS accuracy, the authors may want to consider using TLD-100 as the reference to compare against for both Gr-200 and TPS methods, as long as sufficient justification is provided as to why TLD-100 dosimetry can serve as the reference dosimetry.

**Answer: We would to thank about your worth comment and consideration. In the new version, we revised the title and whole text following your first point. In other words, we wanted to have a comparison between the TPS calculation and TLD measurements to use the TLD dosimetry as an appropriate quality assurance method for TPS dose calculation.**

Specific Comments:

Line 11: "Entrance skin dose" (ESD) should be replaced by "skin dose" or "exit skin dose" here and throughout the manuscript. For prostate brachytherapy, the radiation is emitted from a source inside the patient body and then reaches the skin, so the use of "entrance" is not accurate.

**Answer: As you suggested, we have revised the whole text, in a way that "ESD" replaced with "skin dose".**

Line 59: "~1.25 MV" uses an inaccurate unit, MV. The unit should be MeV instead for the gamma emission energies of Co-60.

**Answer: You are right. The correction was done in the text.**

Line 69: "corporation" should be "cooperation" or "participation".

**Answer: It was carried out in the new version.**

Lines 81-84: The TLD calibration setup appears to have two potentially significant deviation from the actual measurement setup:

1) Angular geometry: the calibration takes place at 100cm distance to the TLDs, i.e. perpendicular irradiation, whereas the actual measurement setup involves much shorter distance in the patient body. Can the authors please address the concern of potential angular response dependency issues with the TLD chips?

**Answer:** Thanks for your comments. You are right. The output of the machine was measured by a calibrated chamber at 100cm in perpendicular condition. We did not investigate the different angular response of the TLDs, because following the previous studies the uncertainty of TLDs at different angles is negligible.

**For example in this study: A comparative evaluation of luminescence detectors: RPL-GD-301, TLD-100 and OSL-AL2O3: C, using Monte Carlo simulations, the authors expressed that the variations in sensitivity for angles up to  $\pm 80$  degrees from the central axis of the beam were less than 1.5%.**

2) Backscatter: the calibration takes place with 5cm of Perspex phantom for backscattering, whereas the actual measurement setup does not have any backscattering. Can the authors please address the discrepancy in the backscattering environment as well as the adequacy of calibration setup?

**Answer:** Dear reviewer, backscatter radiations have lower energies than the primary one, however, previous studies reported that TLDs dependency related to the energies is negligible, therefore, backscatter is not a remarkable factor. For example the following studies stated that the energy dependence of the luminescent dosimeters are less than 2.2%.

1. A comparative evaluation of luminescence detectors: RPL-GD-301, TLD-100 and OSL-AL2O3:C, using Monte Carlo simulations
2. Evaluation of Effective Sources in Uncertainty Measurements of Personal Dosimetry by a Harshaw TLD System

Line 105: Please spell out and clarify "EQD2".

**Answer:** It was clarified in the new version.

Lines 117-119: Please identify small-letter, n. Is it the same as N?

**Answer:** n and N is the same, therefore, we have written 'N' in the equation and text.

Line 127: the reference #16 appears to be an typo, please provide the correct reference number.

**Answer:** Thanks for your consideration. The correct reference was cited.

Lines 163-168: Three occurrences of "deference" should be changed to "difference".

**Answer:** Thanks a lot for your consideration. The relevant correction has been done in the new version.

Lines 169: What makes the TPS dose the "reference dose"?

**Answer:** In the new version we have mentioned that in this study we just compared the two TLDs with TPS calculation. Thus, the whole text has been edited following this comment and your first comment.

Line 210: Invalid Citation.

**Answer:** Since the reference was missed, it was corrected.

Table 2: The data presentation is confusing, are the two numbers in each field meant for TLD-100 and GR-200, respectively? If that is the case, listing the values in a new column for GR-200 will be better.

**Answer:** Since the data of table 2 seems to be confusing, we have prepared another column for GR-200.

Table 2: Please explain why the uncertainty for Holder correction factors ( $F_{hol}$ ) are different for TLD-100 and Gr-200.

**Answer:** The difference of  $F_{hol}$  between the two TLDs can be related to the different dimensions of the TLDs. Dimensions of TLD – 100 are more consistent with holes' dimensions.

Figure 2: Why are the horizontal axis "Dose (cGy)", is that the un-corrected dosimeter reading? Please clarify in the manuscript and/or the Figure title.

**Answer:** The horizontal axis is TLD output, therefore, it was revised in the figure. Thanks a lot for your comment.

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Reviewer 4

#### INTRODUCTION:

The first paragraph may be changed to,  
Prostate cancer is the second common cancer in the world among men and constitutes fifth most common cause of death (1). Very few patients are diagnosed with less than 50 years and most of them are diagnosed after 65 years. The cumulative risk of prostate cancer ranges between 0.5 to 20% worldwide at the age of 85 years (2).

**Answer:** Dear reviewer, we would like to appreciate your worth suggestion. The above-mentioned sentences were revised based on your corrections.

#### MATERIALS & METHODS:

First sentence needs to be changed. The study is carried out with BEBIG HDR machine. Why the authors mentioned Microselectron? (LINE 63-65).

**Answer:** The relevant sentence was revised and we eliminated "Microselectron" in the new version. Because it is another machine and we wrote it wrongly. Thanks a lot for your consideration.

Line 69- Corporation needs to be changed into co-operation.

**Answer:** It was carried out in the text. Thanks a lot for your consideration.

Line 71-73 - The phosphor and the impurities in TLD 100 and GR -200 needs to be mentioned correctly.

**Answer:** We have checked the material of the two TLDs and revised the relevant corrections.

Line 105-106 - At what depth skin dose was estimated? The depth at which TLD dose measured and TPS dose calculated to be mentioned.

**Answer:** In the new version we added a section “skin dose measurement”, and we explained the depth of TLD dose measurement and other relevant explanations.

Line 113: Instead of pelvic, pelvic bones to be mentioned.

**Answer:** We replaced “pelvic bones” instead of “pelvic” following your suggestion.

Line 124: All components in equation 2 to be mentioned and their values needs to be specified.

**Answer:** The abbreviations related to equation 2 and their values used by the previous study have been clarified in the text.

#### RESULTS:

Line 147: Instead of the mentioned energy range dose range has to be incorporated.

**Answer:** You are right. In the new version we mentioned dose range instead of energy range.

The calibration co-efficient estimated for GR -100 in the present study is 0.0022 as against the reported value in literature 4 to 4.5. (Altaf et al (13). Needs clarification for this significant variation.

**Answer:** In Altaf et al (13) study, the energy ranges and consequently doses are completely different with our study, therefore, the co-efficient factor has a big variation. The relevant explanations were added in the text and highlighted.

It was observed that the calculated and estimated dose for lateral sides vary much compare to the anterior side. What could be the reason for such variation?

**Answer:** The reason is “in the anterior points the distances from the sources are lesser than lateral points”. We have stated this reason in the text.

In the Results section it was mentioned that 70% of measurements were in good agreement with TPS calculated values. Whereas in conclusion section, it was indicated that 96% of measured and calculated values were in good agreement. This needs clarification.

**Answer:** The 70% written in the result section is correct. It was mistakenly written 96% in conclusion section. Therefore, the relevant correction has been done. Thanks a lot for your consideration and dedicating your worth time.

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2<sup>nd</sup> Editorial decision  
21-Nov-2020

Ref.: Ms. No. JCTRes-D-20-00103R1

A comparison of skin dose estimation between thermo-luminescent dosimeter and treatment planning system in prostatic cancer: a brachytherapy technique  
Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger  
Editor-in-Chief  
Journal of Clinical and Translational Research

Comments from the editors and reviewers:

Reviewer #2: Revision is considered satisfactory.

Reviewer #3: The revised manuscript and individuals responses successfully addressed my initial comments and questions. Thank you.