Journal of Clinical and Translational Research
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Role of stone heterogeneity index in determining success of shock wave lithotripsy in urinary calculi

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Handling editor:
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Editorial decision: 23 January, 2021
Revision received: 28 January, 2021
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1st Editorial decision
27-Sep-2020

Ref.: Ms. No. JCTRes-D-20-00070
Role of stone heterogeneity index in determining success of shock wave lithotripsy in urinary calculi
Journal of Clinical and Translational Research

Dear Dr Iqbal,

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.

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 Oct 27, 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 #2: This manuscript investigated the impact of several factors measured by non-contrast CT on the outcome of the shock wave lithotripsy. A new factor, stone heterogeneity index (SHI) raised special attention recently and may have an impact on stone free rates. The results showed the stone density, stone index of stone heterogeneity (SHI), and length of the stone were significantly different between the stone free and residual stone group. They concluded SHI can be a helpful CT scan-based parameter to assess stone fragility.
Overall, this is an interesting article.
Here are my concerns:
1. Since stone heterogeneity index is a new parameter, the authors should describe more details of how to determine this parameter.
2. A representative photography to show how to measure stone density, stone heterogeneity index and skin stone distance is essential.
3. In table 2, the SHI value in 5-10 mm stone size and stone failure group iseven higher than 10-15 mm stone size and stone free group (218 vs 210). Is there any good explanation?
4. As mentioned by the authors, is there any suggested SHI cut-off value to predict success stone treatment?

Authors' response

Reviewer comments and queries:-

Ref.: Ms. No. JCTRes-D-20-00070

(Journal of Clinical and Translational Research)

Title:- Role of stone heterogeneity index in determining success of shock wave lithotripsy in urinary calculi.

Dear team,

We are thankful to the reviewers for guiding us to further polish our manuscript.

Worthy reviewers have ask certain points which are answered point wise below,

Reviewers' comments and point wise answers:

Reviewer #2:

1. This manuscript investigated the impact of several factors measured by non-contrast CT on the outcome of the shock wave lithotripsy. A new factor, stone heterogeneity index (SHI) raised special attention recently and may have an impact on stone free rates. The results showed the stone density, stone index of stone heterogeneity (SHI), and length of the stone were significantly different between the stone free and residual stone group. They concluded SHI can be a helpful CT scan-based parameter to assess stone fragility. **Overall, this is an interesting article.**

1. We are thankful for the encouraging comments by the honorable reviewer. It really gives us an extra energy and motivation to follow the journey of research.

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2. **Since stone heterogeneity index is a new parameter, the authors should describe more details of how to determine this parameter.**

Reply to query:- Dear editor , it was a good query by honorable reviewer. for assessing the skin-stone distance we followed the methodology portrayed by Pareek et al. Computation of mean stone density (mean value of the Hounsfield units) was accomplished on an axial image (computed tomography) by generating elliptical region of interest on the CT scan ,portraying stone in its longest dimension. Special attention was given not to include any soft tissue while measuring the stone density (12).

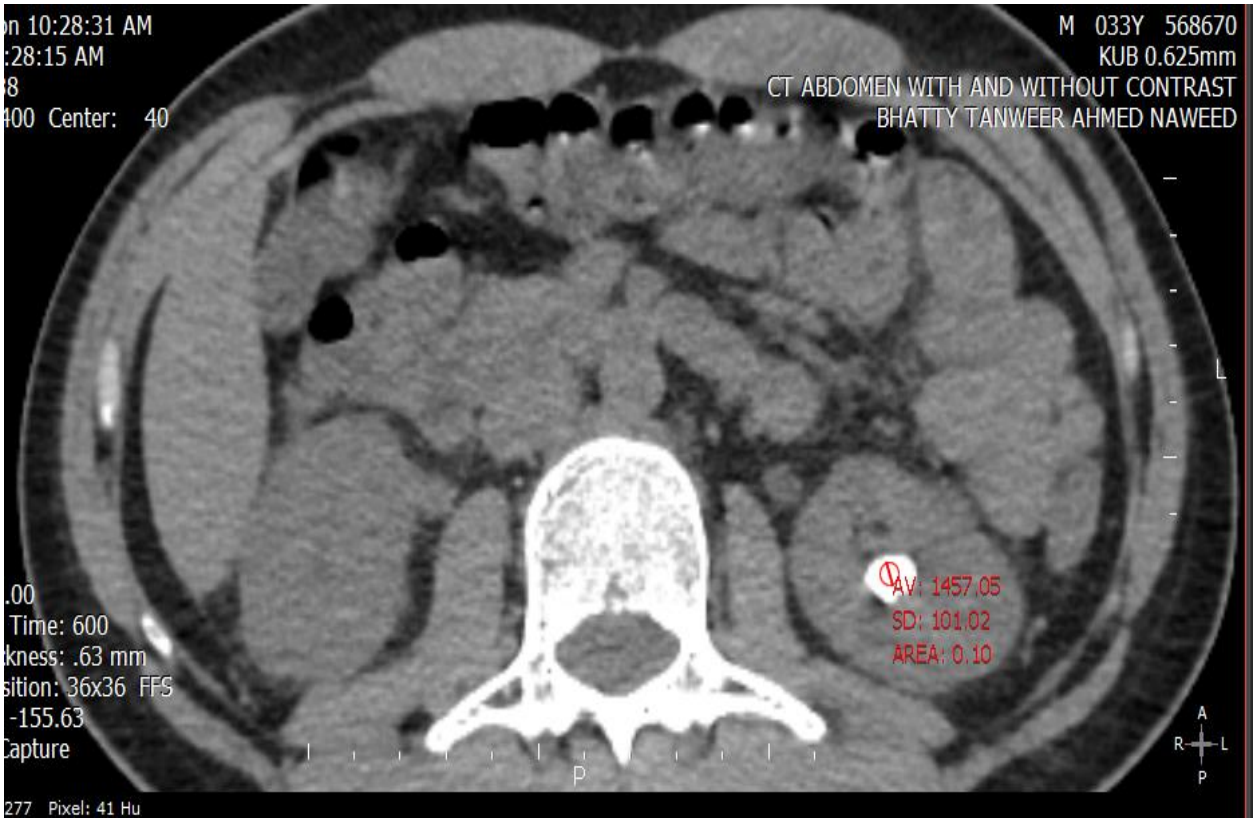
Mean density of stone (MSD) was described as the mean value of Hounsfield's Units in the region of interest, while stone heterogeneity index (SHI) was designated as the standard deviation value of Hounsfield's Units in that same specified region of interest (11). Please note in the picture below, An elliptical area over the stone (red colored) on axial view of Non

contrast CT scan is showing mean stone density of 1457.05 (written in red color) while below it is mentioned the standard deviation of density 101.02 (written in red color).

Hence, Stone density and stone heterogeneity index (SHI) can easily be obtained in a specified stone area that can be easily determined from non-contrast computed tomography (NCCT) using a picture archiving and communication system (PACS).

Ref 11. Lee JY, Kim JH, Kang DH, Chung DY, Lee DH, Jung HD et al. Stone heterogeneity index as the standard deviation of Hounsfield units: A novel predictor for shock-wave lithotripsy outcomes in ureter calculi. Sci. Rep.2016:6;23988; doi: 10.1038/ srep23988.

Ref 12. Pareek G, Hedican SP, Lee FT Jr, Nakada SY. Shock wave lithotripsy success determined by skin-to-stone distance on computed tomography. Urology 2005; 66:941–944.



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3. A representative photography to show how to measure stone density, Stone heterogeneity index and skin stone distance is essential.

Reply to query:- Dear editor , We have added the representative photography to show how to measure stone density, stone heterogeneity index and skin stone distance, as advised by respectable reviewers.

Mean stone density and standard deviation of stone density (also called stone heterogeneity index) are portrayed in figure (1).

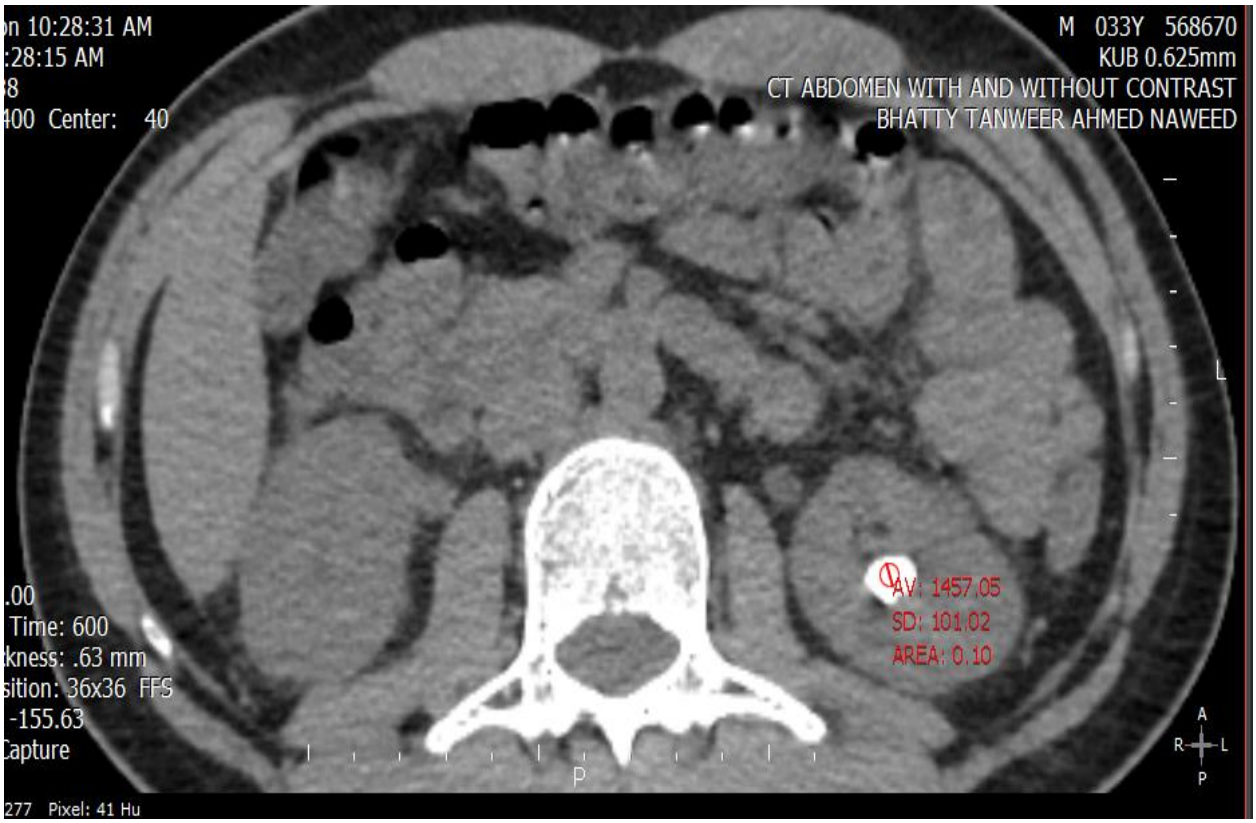

Figure 1:- Mean stone density and standard deviation of stone density (also called stone heterogeneity index) in red elliptical area on axial view of CT scan.

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For measuring skin to stone distance (SSD) we utilized method as portrayed in figure 2 (figure 2A, B, C). Average of skin to stone distance measured at three angles (0°, 45, and 90°) was considered as the skin to stone distance.

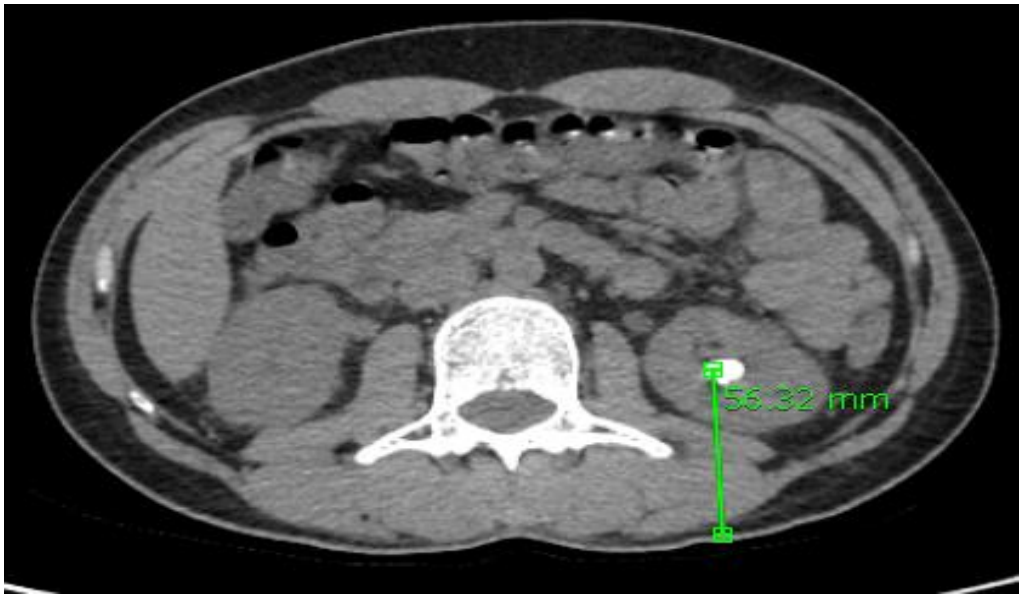

Figure 2A:- The computation of skin-to-stone distance at 90° on an axial scan of non-contrast computed tomography. SSD: skin to stone distance.

Figure 2B:- The computation of skin-to-stone distance at 45° on an axial scan of non-contrast computed tomography. SSD: skin to stone distance.

Figure 2C:- The computation of skin-to-stone distance at 0° on an axial scan of non-contrast computed tomography. SSD: skin to stone distance.

Average of skin to stone distance measured at three angles (0°, 45, and 90°) was considered as the skin to stone distance.

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4. In table 2, the SHI value in 5-10 mm stone size and stone failure group is even higher than 10-15 mm stone size and stone free group (218 vs 210). Is there any good explanation?

Reply to query:- Dear editor, it was a nice pointing of the fact by honorable reviewer. Size of stone cannot affect the density and so subsequently the standard deviation of stone. It is rather primarily the density of stone that matters more than the size of stone when both are taken into consideration and it has been seen in recent literature that stone size, density and skin

stone density, all together have a composite effect on stone free rates of stone subjected to lithotripsy (1, 2, 3). It may also be due to the reason that stone densities were almost similar in the different stone size sub groups in our study, so averting the compounding factor or bias which could have arisen by the differing stone densities among these stone size subgroups. Focus in this paper was more on the stone density and its deviation (SHI). Size has effect on stone free rate in larger stones (1, 2, 3). Interestingly ,in smaller stone size subgroup (5-10 mm) the effect of density and subsequently the SHI is offset to some extent due to the smaller size of stone that goes in favor of more stone free rates as described in literature (1,2).

References:-

1. Tran TY, McGillen K, Cone EB, Pareek G. Triple D Score is a reportable predictor of shockwave lithotripsy stone-free rates. J Endourol 2015;29:226–230.

2. Gökce MI, Esen B, Gülpınar B, Süer E, Gülpınar Ö. External Validation of Triple D Score in an Elderly (≥65 Years) Population for Prediction of Success Following Shockwave Lithotripsy. J Endourol.2016;30:1009-16.

3. Ozgor F, Tosun M, Kayali Y, Savun M, Binbay M, Tepeler A.External Validation and Evaluation of Reliability and Validity of the Triple D Score to PredictStone-Free Status After Extracorporeal Shockwave Lithotripsy. J Endourol. 2017.31:169-173.

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5. As mentioned by the authors, is there any suggested SHI cut-off value to predict success stone treatment?

Reply to query:- Dear editor, No cut off value has been found however it needs multi institutional studies before recommending one. Other reason is that we had analyzed effect of SHI in different stone density and stone size sub groups. We need multi institutional prospective randomized controlled studies to find cut off values based on a nomogram that

incorporates the SHI value as well. Otherwise, if SHI cut off value is used alone without keeping in mind the effect of differing stone sizes and densities then it may not be that much beneficial. This study open our eyes to the fact that caution has to be exercised while utilizing the SHI values in different stone sizes and densities subgroups. In a nutshell, we need a nomogram for that purpose wherein we can judiciously incorporate well calculated Cut off values of SHI for each subgroup of stone densities and stones sizes.

As advised by the honorable reviewer, after generating ROC curves, a cut off value for SHI was found to be 213.Its sensitivity being 0.67 and specificity 0.60. AUC was 0.60 (CI 0.531-0.673), which demonstrated greater sensitivity and specificity values.

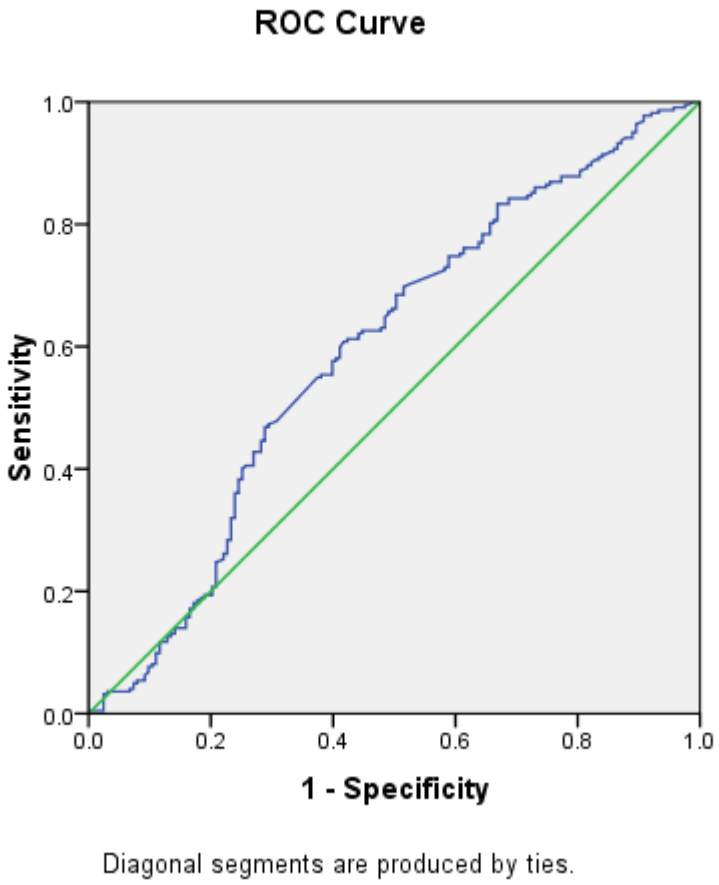

Figure 3: Receiver operating characteristic of Stone heterogeneity index (SHI) for shock wave lithotripsy success.

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We are much thankful to the reviewer for the hard work and giving their precious time for guiding us.

2nd Editorial decision
20-Nov-2020

Ref.: Ms. No. JCTRes-D-20-00070R1
Role of stone heterogeneity index in determining success of shock wave lithotripsy in urinary calculi
Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at http://www.jctres.com/en/author-guidelines/ under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Dec 20, 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:

Dear authors,

Your manuscript has successfully passed through peer review, and can be accepted for publication. Before I can do so, however, I must ask you to have your manuscript proofread by a native speaker who understands the field and therefore can correct some of the syntax errors as well as grammatical and spelling mistakes.

I would like to point to our author guidelines, where we explicitly indicate that all manuscripts must adhere to academic level English before we can accept them.

https://www.jctres.com/en/author-guidelines/

If you cannot find a suitable native speaker and expert, please let us know.
We have qualified academics in our editorial team who could help for a fee.

Kindest regards,

Michal Heger, editor

Authors' response

Reviewer comments and queries:-

Ref.: Ms. No. JCTRes-D-20-00070

(Journal of Clinical and Translational Research)

Title:- Role of stone heterogeneity index in determining success of shock wave lithotripsy in urinary calculi.

Dear team,

We are thankful to the reviewers for guiding us to do only few minor revisions to further polish our manuscript.

We have been encouraged much by their comments that it is acceptable manuscript.

Worthy reviewers have said to get it proof read in order to rectify minor syntax, grammar and spelling mistakes.

Reviewers' comments and point wise answers:

Reviewer :

Your manuscript has successfully passed through peer review, and **can be accepted for publication**. Before I can do so, however, I must ask you to have your manuscript proofread by a native speaker who understands the field and therefore can correct some of the syntax errors as well as grammatical and spelling mistakes.

We are thankful for the encouraging comments by the honorable reviewer. It really gives us an extra energy and motivation to follow the journey of research.

We have revised the grammar and have applied the minor corrections needed in the manuscript as highlighted in yellow color.

Punctuation commas have been added where grammatically appropriate (commas highlighted).

Use of appropriate articles the and a and an have been added where appropriate.

Spelling corrections have been applied where needed.

Some sentences have been rearranged as can be seen yellow highlighted areas.

Please do not hesitate to contact us If you have any queries.

Many regards

3rd Editorial decision
23-Jan-2021

Ref.: Ms. No. JCTRes-D-20-00070R2
Role of stone heterogeneity index in determining success of shock wave lithotripsy in urinary calculi
Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at http://www.jctres.com/en/author-guidelines/ under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Feb 22, 2021.

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:

Dear authors,

Thank you for submitting your revised paper and for trying to implement my comments.

Unfortunately, you have not complied with my request to have the paper proofread by a native speaker. I know this because the paper contains numerous syntax errors that a native speaker would never make.

So we can do one of two things. First, you can submit the paper for language polishing by a paid service. Alternatively, I ask one of our board members to help you with the language in exchange for a fee or co-authorship on the paper.

Please let me know what you decide.

Thanks,

Michal Heger
Editor

Authors' response

Reviewer comments and queries:-

Ref.: Ms. No. JCTRes-D-20-00070
(Journal of Clinical and Translational Research)

Title:- Role of stone heterogeneity index in determining success of shock wave lithotripsy in urinary calculi.

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Spelling corrections have been applied where needed.
Some sentences have been rearranged as can be seen yellow highlighted areas.

Please do not hesitate to contact us If you have any queries.

Many regards

4th Editorial decision

Ref.: Ms. No. JCTRes-D-20-00070R3
Role of stone heterogeneity index in determining success of shock wave lithotripsy in urinary calculi
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: