We thank the reviewer for the positive assessment of the work and appreciate the time and effort invested.

All the corrections that were added into the manuscript according to the Reviewer suggesting were highlighted with yellow.

Major revision:

Comments 1: The authors evaluated the mechanical properties of the cell-soft-hydrogel system at non-invasive nanoscale resolution using scanning ion conduction microscopy. In simple terms, the authors should just use the microscope to show the mechanical properties of cells in different states (culture dish and hydrogel), so what is the significance? What can we do with all this data? Can it be used as an indicator of key behaviors? The authors are invited to explain in detail.

Response 1:

The aim of this article was not to obtain indicators of the key behavioral parameters of MCF-7 cells adhered to self-assembling peptide hydrogels, but rather to explore what new possibilities or information the alternative Scanning Ion-Conductance Microscopy (SICM) method can provide compared to the traditional Atomic Force Microscopy (AFM) method in studying the mechanical properties of the cell-hydrogel system. To the best of our knowledge, there are no studies that have produced maps of the mechanical property distribution of cell-hydrogel systems where the substrate is softer than the cell itself. Such systems might be of interest in the field of regenerative medicine for the restoration of soft tissues, such as soft brain tissue, E ~ 0.1-1 kPa, or adipose tissues E ~ 1-2 kPa. The use of this method allowed us, firstly, to simultaneously obtain a distribution map of both the soft hydrogel and the living cell. Such measuring gives the opportunity to examine the immediate change of cell's mechanical properties in response to scaffold behavior, which is important in the field of regenerative medicine when testing the effects of different drugs on the cell-scaffold system. Secondly, the measurements carried out with SICM were in agreement with the AFM technique. One of the main advantages of SICM over AFM is its non-invasiveness; therefore, the data obtained in this study suggest that the SICM method can be used as an independent method for measuring the mechanical properties of the cell-soft hydrogel system. Thanks to its non-destructive nature, it allows for the investigation of the dynamics of the same cell on the hydrogel over a long period, which cannot be achieved with the traditional AFM method. This capability is also important for obtaining more accurate information about changes in cell metabolism during their interaction with the scaffold. Furthermore, studies using confocal microscopy showed that the mechanical property distribution map of the cell on the hydrogel obtained by the SICM method describes specific cellular structures (nucleus/cytoskeleton), allowing for a more detailed description of changes in cell biomechanics during interaction with the hydrogel.

These considerations were added to the Conclusions section.

Comments 2: In Section 2.1, using SICM to evaluate the mechanical properties of the cell-hydrogel system, the authors only describe the relevant parameters obtained without specific explanation. What is the use of these data after we obtain them? Can these data be used to evaluate the hydrogel model? Or is there some other use? And then there's Section 2.2.

Response 2:

The data obtained in Section 2.1 were used to assess the adequacy of the alternative SICM method compared to the traditional AFM method for determining the mechanical properties of the cell-soft hydrogel system. By comparing the data from Section 2.1 and Section 2.3 in the Discussion section, it is concluded that this method correlates well with the AFM method, which allows for the advantages of the SICM method over the AFM method to be utilized in the study of the biomechanics of live cells adhered to scaffolds. The additional information obtained using the SICM method compared to AFM and its potential applications are described in the Conclusion section.

Section 2.2, as mentioned at the beginning of the section, is dedicated to investigating whether the mechanical property distribution maps obtained using the SICM method correspond to real organelles in cells. The obtained data can be used to investigate the more detailed response of cells to the influence of scaffolds on them.

Explanatory information has been added at the end of Sections 2.1, Discussion and Conclusion sections.

Comments 3: It can be seen from the title that the author mainly uses some technical means to evaluate the resolution of hydrogels. What is the purpose of the tests in parts 2.4, 2.5 and 2.6? What is the relevance to the subject? These are some of the common reported preparation methods and related properties of hydrogels. Please explain in detail.

Response 3:

The primary research in this article focused on studying the mechanical properties of the cell-soft hydrogel system using the SICM method and comparing the obtained data with those from the traditional AFM method. However, a logical continuation of this research is the study of the self-assembling hydrogel to investigate its biocompatibility with living cells, with the aim of using it as a scaffold in regenerative medicine in the future.

When studying the biocompatibility of hydrogels with cells, there is a set of scaffold characteristics that can directly affect cell viability on them. These characteristics include the swelling and degradation of hydrogels. These properties are important because the hydrogel is intended to mimic the extracellular matrix, which is largely composed of water.

Section 2.5 is dedicated to the test that describes the biocompatibility of the self-assembling gel and living cells, which is a necessary experiment when proposing a hydrogel as a scaffold.

Since section 2.5 demonstrated low biocompatibility of the Fmoc-FF hydrogel with cells, the question arose whether this result is due to the method of hydrogel preparation (which could be adjusted to improve the biocompatibility of the gel and cells) or if it is a consequence of the peptide composition of the hydrogel. This was investigated in this section.

The explanations have been added to sections 2.4-2.6.

Minor revision:

Comments 1: The way in which the author uses the number of figures in the text is inconsistent, such as fig.xx, Figure xx, Fig.XX, Fig Xx, Fig xx(A), Fig xxA. Some lack space. This problem appears many times in the main text, please correct it.

Response 1:

This problem was corrected.

Comments 2: In Figure 1, there is no G, I in the number. The numbering order and the back and forth order of the text description are also inconsistent. The numbers of B and D are in the interior of the figure and are not clear. Suggestions are written outside the picture. You inserted a picture in C, and I'm sure you can add a number as well. In J, the author describes its bimodal nature, but it is not very clear, which may be overlap and color occlusion. It is suggested to divide it into three separate figures in SI.

Response 2:

Figure 1 and its numbering order was corrected. To clarify the bimodal nature of system the Fig. 1H was divided into three separate figures and also presented in SI, see Fig. S3.

Comments 3: Figure 2. The size of the picture is inconsistent, and the scale bar does not appear in the explanation.

Response 3: The scale bar was added to Figure 2 and to the explanation of this Figure.