Reply to reviewer 02544209

We thank the reviewer for the useful advises.

1) The reviewer asked a little information about qPCR method.

We added little information about qPCR methodology in the paragraph "Circulating cell-free DNA and qPCR measurement"

2) The reviewer asked separate the main text into sections

We separated the main text into more paragraphs to facilitate readership as follow:

INTRODUCTION; Circulating cell-free DNA and qPCR measurement; Quantification of total circulating cell-free DNA; Quantification of cell-free DNA integrity; Discussion; Conclusion.

3) The reviewer asked to add some information on the sensitivity of specificity of ALU-based PCR in different clinical settings.

We inserted observations about sensitivity and specificity of ALU-based qPCR in the different clinical settings in the discussion section.

4) The reviewer asked to correct "According to Umetani et al., Agostini et al. using the same ALU247bp" with "Accordingly to Umetani….."

We made corrections to English misspelling.

We would like to point out that the manuscript has been improved by giving useful information for an easier comprehension for the readers and by adding the most recent literature of 2018, which was published in the meantime.

To facilitate the reviewer we highlighted the changes in the text in blue.

eply to reviewer 02682232

The reviewer asked to add diagrams of literature meta-analyzes and to add basic principles of free cell DNA.

As suggested by the reviewer, who we thank for the kind consideration, we added the diagrams (indicated as Figures 1 and 2) to better explain the main theoretical points of circulating free DNA and to summarise the results from literature on BC patients versus Healthy females.

We would like to point out that the manuscript has been improved by giving useful information for an easier comprehension for the readers and by adding the most recent literature of 2018, which was published in the meantime.

To facilitate the reviewer we highlighted the changes in the text in blue.