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Reviewer #1

Scientific Quality: Grade C (Good)

Specific Comments to Authors: The authors used contrast-enhanced ultrasound (CEUS) to study the colorectal tumor vasculature and the correlation with angiogenesis and prognostic significance, which is a powerful tool for the clinical imaging. After reasonable grouping the patients based on the TNM staging system, the authors showed that quantitative parameters, including peak intensity (PI), time to peak (TTP), and area under the curve (AUC), are significantly related to VEGF expression and microvessel density. This result also draws a conclusion that CEUS has a high potential in guiding treatment planning and predicting patient outcomes. In short, the topic of this manuscript is timely and interesting. The authors have organized the manuscript rationally, with good methodology and well-written English. However, some important editing needs to be done before publication: 1) The percentage of VEGF-positive tumor cells and CD34-positive microvessels are crucial in this study. What method did the author use to count the positive objectives? 2) The percentage of patients' age ranges are also important data that should be present in Table 1.

Thank you for your comments and suggestions. We have revised our manuscript accordingly. We have added the method of counting the percentage of VEGF-positive tumor cells and CD34-positive microvessels to the methods section, and the percentage of patients' age ranges to Table 1. We hope that our revisions have addressed your concerns.

Reviewer #2

Specific Comments to Authors: Contrast-enhanced ultrasound (CEUS) is a promising way for colorectal cancer (CRC) imaging due to its potential in evaluating tumour blood flow and vascularization. In this study, the authors aimed at quantitatively evaluating



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the colorectal tumour vasculature with CEUS, and exploring the correlation between colorectal tumour vasculature and angiogenesis makers. The authors used primary clinical data, CEUS image analysis, and immunohistochemical analysis to verify their hypothesis. The results showed that CEUS parameters, such as peak intensity (PI), time to peak (TTP), and area under the curve (AUC), are significantly correlated with VEGF expression and MVD. So, in my opinion, this paper is well-written. The experiment design is reasonable, and the results reflects the conclusion as well. I recommend its acceptance after the minor revision. The detailed comments are: 1. Since CEUS is a relatively novel imaging technique, what are the common imaging methods before it? Compared with these methods, what is the key advantage of CEUS? 2. Several grammar issues should be solved. For example, "Contrast-enhanced ultrasound (CEUS) is a non-invasive, safe, and cost-effective method for evaluating tumour blood vessels, which play a crucial role in tumour growth and progression" Herein, which should be replaced by that.

Thank you for your positive comments and feedback. We have revised our manuscript accordingly. We have added a paragraph to compare CEUS with other imaging methods in the introduction, and corrected the grammar errors in the manuscript. We hope that our revisions have satisfied your expectations.