Reviewer’s report

Title: 3-D reconstruction of a human foetus with combined holoprosencephaly and synophthalmia

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Reviewer: Shigehito YAMADA

Reviewer’s report:

This manuscript describes fetal holoprosencephaly, a rare condition of congenital anomalies. The authors made detailed anatomical analysis using 3D reconstruction. The findings described in this paper are thought to be important to understand pathogenesis of holoprosencephaly.

Minor Essential Revisions

Materials and Methods
1. “A Nikon Coolpix 8400 camera with a resolution of 8 mega pixel”
This part means only commercial specs of the camera. Resolution should be described as X micron/pixel or something.

2. “Digitizing a single section took between 5 and 30 minutes…”
This part may not be required because it depends on the spec of the computer how it takes to digitize.

3. “By freezing and thawing single structures (electronic dissection)”
Does it mean analysis has been done on the software? Or do the authors freeze and thaw the sections?
Although the electronic dissection from 3D dataset may be well-known technique among the authors, an appropriate reference should be inserted.

Results
4. There are a lot of Figure number (1-9), but each figure has only two or three images (sometimes only one). Those figures should be put together.

5. Page 6: (Fig 1a) may be (Fig 1a and 1b), and (Fig 1b) may be (Fig 1c).

6. Page 6: “fife” should be “five”.

7. “histological” should be “histologically”.

8. Fig 4 and Fig 5 show abnormal bone structures of this case. Readers don’t always have enough knowledge about the normal fetal bone structure at 20 weeks of gestation, therefore control data or reference should be required.

9. In the reviewer’s PC, Fig 8b was not displayed correctly; arrow and alphabets
may be placed in the wrong position.

Discussion

10. “but also environmental influences have been implicated”
This phrase requires some references.

11. The third paragraph is about arterial malformation, however, it is only the enumeration of the findings. Something discussed should be required.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.