Peer Review File

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1. Please comment if the device is approved (CE or FDA approval) and if it is commercially available.

Reply 1: Thank you for your remark regarding CE certification of the CeraFlex occluder. We added the information that the occluder is commercially available in Europe.

Version of first submission	**Changes**	**Where**
The CeraFlex™ ASD occluder (Lifetech Scientific Co, Shenzhen, China) is a self-expanding double-disk device made from a nitinol wire mesh that has been available in Europe since its CE certification in 2013.	The CeraFlex™ ASD occluder (Lifetech Scientific Co, Shenzhen, China) is a self-expanding double-disk device made from a nitinol wire mesh that has been commercially available in Europe since its CE certification in 2013.	Introduction Page 4; line 15

2. It would be better to compare with Amplatzer Occluder from existing or your own data so that the efficacy could be further enhanced.

Reply 2: Thank you for your remark regarding our study. However, we have to admit that this study was a single-arm CeraFlex implantation study. In the discussion of our manuscript page 10 line 11 and 12 the sentence "In the Amplatzer septal occluder instructions for use Amplatzer implantation is not recommended if the interatrial aortic rim is < 5mm in any echocardiographic transesophageal plane, to avoid aortic erosion"was omitted, since by now the instruction for use for CeraFlex also require an aortic rim of 5mm. Furthermore, in the following sentences the literature comparing Amplatzer and CeraFlex Device is discussed.

Version of first submission	**Changes**	**Where**
However, the stiff connection of the Amplatzer ASD occluder to the delivery cable may cause difficult device placement, especially in patients with larger ASDs	However, the stiff connection of the Amplatzer ASD occluder to the delivery cable may cause difficult device placement, especially in patients with larger ASDs	Discussion Advantages / features Page 10; line 11-12

and deficient aortic septal rims. In the Amplatzer septal occluder instructions for use Amplatzer implantation is not recommended if the interatrial aortic rim is < 5mm in any echocardiographic transesophageal plane, to avoid aortic erosion. Just recently Abbott introduced a more flexible delivery cable (Treviso) [17], which improves the flexibility at device delivery.	and deficient aortic septal rims. ~~In the Amplatzer septal occluder instructions for use Amplatzer implantation is not recommended if the interatrial aortic rim is < 5mm in any echocardiographic transesophageal plane, to avoid aortic erosion.~~ Just recently Abbott introduced a more flexible delivery cable (Treviso) [17], which improves the flexibility at device delivery.	

3. Please further provide more detailed eligibility information on the target population in the abstract.

Reply 3: We added eligibility information on the target population in the abstract and considered the number of words.

Version of first submission	**Changes**	**Where**
In total, 103 patients were treated with a CeraFlex™ ASD occluder. Device embolization occurred in two patients (2%).	In total, 103 patients with a hemodynamically significant secundum ASD were treated with a CeraFlex™ ASD occluder. Exclusion criteria were myocardial infarction, unstable angina pectoris, decompensated heart failure, multiple defects, and bacterial and/or viral infection or evidence of intra-cardiac thrombi. Device embolization occurred in two patients (2%).	Abstract: Results Page 3; line 12-15

4. Page 6 lines 1-2 “Interventional procedures were conducted according to instructions for use and the standard approach of the respective study site”, please provide

references for this point. Readers need to know how the standard approaches in the three sites are carried out.

Reply 4: Dear Reviewer, thank you for your second comment. Since this was a post market surveillance study, the local implantation protocol of the three sites were applied. There was no general standard approach.

5. I failed to find information regarding who delivered the intervention. As there're 103 patients from three sites, it is not realistic to report each operators' name. But, information is required to transparently show the operation. For example, what surgeons on the learning curve in each site did the surgery? Is there a big inconsistency regarding background information between surgeons?

Reply 5: Dear Reviewer, thank you for your comment. All implanters are experienced pediatric cardiologists. All interventionalists had long lasting experience with several different ASD occlusion devices.

6. I failed to find how long was it intended to take to deliver the intervention to each unit on page 6, lines 1-19.

Reply 6: Dear Reviewer, thank you for your comment. The day before the intervention the patients were admitted to the hospital and the day after the intervention the patients were discharged.

7. Though this is a single-arm clinical trial, the authors should explain how the initial sample size (N=148) was determined. I understand that the authors collected data between April 2016 and December 2019. But this timespan?

Reply 7: Dear Reviewer, thank you for your comment. The goal was to treat a total of 100 patients with a CeraFlex device in the three study sites. Due to organizational reasons and because the inclusion criteria could not be met in all cases, our target was reached in December 2019.

8. The baseline data in table 2 is too simple. Please also consider adding more relevant information to atrial septal defects, such as blood pressure, ejection fraction etc.

Reply 8: Dear Reviewer, thank you for your comment. We added information about the defect size in table 2. The size of the implanted devices can be found in figure 3. Due to the heterogeneity of the patient population (age of inclusion 3 years to 80 years), we do not consider a comparison of blood pressure and ejection fraction to be useful. For example, in contrast to the adult population, the ejection fraction in children is within the normal range.

Table 2: Anthropometric data of patients with a successfully closed atrial septal defect using CeraFlex™ occluder

	Successfully closed ASDs (n=103)		
	M ± SD	Median [IQR 25; 75]	Min / Max
Sex, female	75 (72%)	-	-
Age at procedure, Years	23,36 ± 24,73	9,0 [6,0; 47,0]	3 / 80
weight, kg	42,86 ± 26,69	29,0 [21,0; 64,0]	13 / 120
height, cm	140,23 ± 26,49	135,0 [117,0; 167,0]	97 / 192
Defect size, mm	13,27 ± 4,92	12,0 [10,0; 16,0]	4 / 30

Mean and standard deviation; Median and interquartile [IQR 25; 75].

ASDs: atrial septal defects; kg: kilogram; cm: centimeter; mm: millimeter.

9. Also, in table 2, please consider separating and comparing the baseline data between the 98 participants who completed 6 months follow-up and the 5 dropouts.

Reply 9*: Dear Reviewer, thank you for your comment regarding table 2 and the dropouts.*
Table 2 shows the data of the patients who completed the study and does not contain data of dropouts.
Three of the patients withdrew their consent (two patients were 6 years old and one patient was 20 years old). The study participation of two more patients had to be terminated as their occluders embolized. More detailed explanations of the embolizations can be found in the results on pages 8 and 9 and in the discussion on pages 11 and 12.
We do not see any added value in a comparison of 98 patients who completed the study and 5 patients who terminated the study participation prematurely.

10. Please specify the analysis strategy as "intention to treat" as I found the authors have analyzed all 103 participants, including the 5 dropouts.

Reply 10: Thank you for the advice. We added the information "intention to treat analysis" in the discussion.

Version of first submission	**Changes**	**Where**
This is a German prospective multi-center trial evaluating the efficacy and safety of the LifeTech CeraFlexTM ASD occluder for transcatheter closure in	This is a German prospective multi-center trial evaluating the efficacy and safety of the LifeTech CeraFlexTM ASD occluder for transcatheter closure in	Discussion (first paragraph) Page 9; line 15-18

patients with secundum ASD. The results demonstrate efficient and safe ASDO and extend these positive results to the first visit six months after ASDO.	patients with secundum ASD. The results of this intention to treat analysis demonstrate efficient and safe ASDO and extend these positive results to the first visit six months after ASDO.	

11. Figures are too scattered, especially figure 3-5. I suggest merging them.

Reply 11: Thank you for the remark regarding figure 3-5. We merged these figures as "Figure 3a-c".

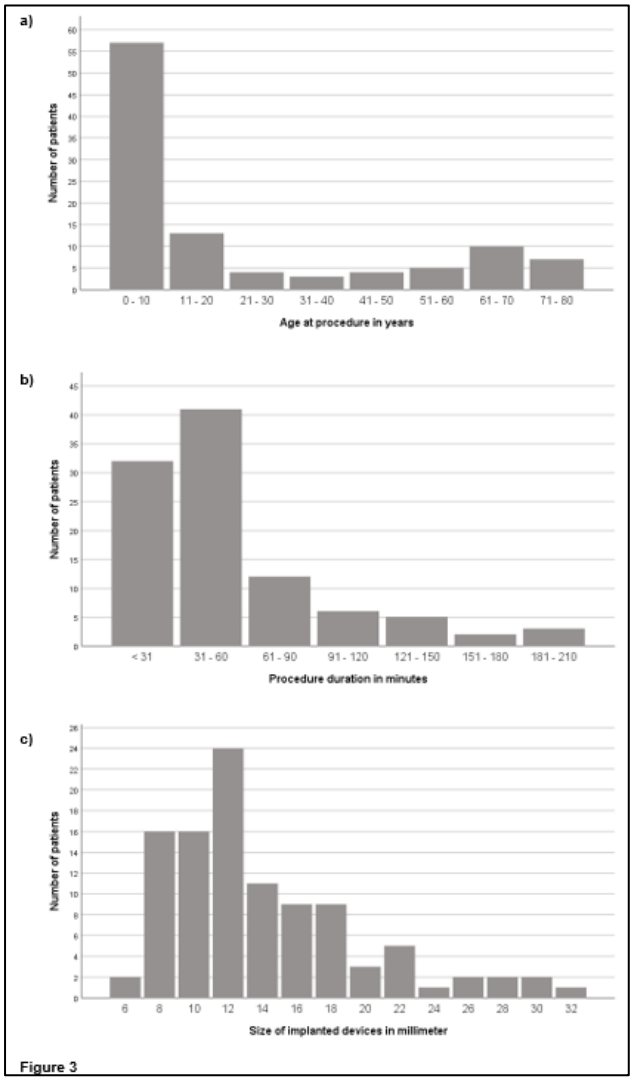

Figure 3