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Development of interatrial shunt implant for the treatment of heart failure

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Abstract
Research in the present study involves the development of an interatrial shunt. The shunt includes a proximal end attached to a disc for supporting a septal wall on the right atrium side, a distal end attached to a flat disc to support the septal wall on the left atrium side, and an intermediate portion connecting the proximal and distal ends that includes a neck portion for providing passage between the left and right atrium of the septal wall. In the proximal, distal and middle portions, the dimensions are selected to provide a low crimp profile ranging from 2-3 mm. Interatrial shunt devices with a unique mechanism to directly reduce left atrial pressures, improve exercise tolerance and potentially improve clinical outcomes and heart failure. As the implant includes the three design such as curvature and flat disc, an implant with barbs and flat disc and an implant with flair and flat disc. The implant with flair and flat disc is flexible to use and easily movable for the implantation.

Keywords: interatrial shunt, left and right atrium, and heart failure

Introduction
The most common heart problem occurs due to increased blood pressure in the left atrium which is unable to accept an adequate volume of the blood at normal diastolic pressure leading to diastolic dysfunction. The heart complication usually is treated using different approaches such as pharmacological treatment as a first line of treatment/surgical treatment. Other treatment, at time, based on its need include implantation of shunt to reduce pressure in the left atrium. A self expandable shunt is mostly placed on the septal wall to create an open passage between the left and right atrium which results in reduction of elevated blood from left atrium to flow towards right atrium due to pressure differentiation. The pressure is reduced in the left atrium and the chances of a heart stroke are minimized. The difference in blood pressure between the two chambers of the heart is referred as the blood pressure gradient. The blood pressure gradient is responsible for the flow of blood from the left to right atrium. The conventional self expandable shunts are used to transfer the blood from left to right atrium at times pose the problem of increased pressure gradient which may lead to detrimental effects in patient. However, the conventional shunts have limited one or two sizes for the treatment i.e., 8 mm hole diameter and 19 mm outer diameter. These limited sizes of the conventional shunts may not fit in accordance with the septal wall of all the hearts. This can lead to stress generation on the septal wall of heart causing damage to the adjacent walls of the heart. As a result, the shunt, after implantation can migrate or deviate from his position due to instability under high blood pressure. The conventional device curvature disc structure at one right atrium end which may pose several disadvantages such as inadequate adherence to the septal wall and device patency may not be maintained to fulfill the requirement. Therefore, there exists a need for an improved interatrial shunt that can overcome limitations of the existing ones.

Material and Methods
The shunt is implanted on a septal wall between a left and right atrium of the heart in a patient. The shunt includes a flared disc on one end, a flat disc on another end and a neck portion between the flared disc and the flat disc. The nitinol tube is subjected to a process of the molding in order to obtain a desired shape of the shunt as per the anatomy of the heart. The self-expandable shunt has a low crimp profile. It may be delivered via the catheter of low profile around 9 to 10 Fr. The shunt crimping profile is in a range of 2-3 mm.
The shunt include a bi-leaflet/ tri-leaflet tissue to provide a unidirectional flow of blood from the left to right atrium and restrict backflow of blood from the right to left atrium of the heart. It was observed that even though, the implant is accommodating well to the septal wall and delivery system is working to a satisfactory; certain modifications to delivery system, deployment mechanism and implant could be done to achieve more accurate and precise results. The process of fabrication of the shunt commences by laser cutting the nitinol tube. The laser cut operation is done over nitinol tube with different designs in order to obtain desired shapes of the shunt. The nitinol tube is laser cut to obtain laser-cut tubes. The laser-cut tube has a proximal end and a distal end. After laser cutting, the laser cut tubes are subjected to a process of grinding and horning. This process is performed in

order to remove the burrs generated during the process of laser cutting. The process of grinding and horning is performed by means of without limitation diamond and/or abrasive gel which clean or remove the burrs generated during the laser cutting to provide a smooth inner surface. The process of molding of the laser cut tubes performed to obtain a desired shape of the shunt. The process of sandblasting preferably performed in order to remove oxidized layer generated on an upper surface of the interatrial shunt during the process of shape setting. The process of electro polishing should also be performed in order to remove the impurities generated during various above processes.

The frame includes a plurality of cells formed by a plurality of strut. The width of the struts in a range of 180-300 µm. The two rows of cells fabricated in any shape such as lotus, cone, and hour glass. The frame includes two rows of cells, one at flair disc and other may constitute the flat disc of the frame. The width and length of the cells found in a range of 2-5 mm and 8-15 mm, respectively. The proximal and distal end is configured to partially engage and protrude beyond the right and left sides of the atrial septum upon implantation. The shape of the shunt is easily loaded in the catheter. The flair disc at the proximal end and the flat disc at the distal end include an outer diameter. The inner diameter and length of the intermediate region is in range of a 6-9 mm and 6-12 mm, respectively. The distal end and the intermediate region of the shunt include a plurality of cavities. The cells constituting the flair disc at the proximal end and the cells constituting the flat disc at the distal end may be aligned at a predefined angle of inclination. The angle of inclination between the flair disc and the flat disc is in range of 40-80 degree. The angle of inclination may depend upon the thickness of the septal wall.

The shunt made in wide ranges of sizes that comply with the dimension of the atrial septal wall of the heart. The increasing range of the inner and outer diameter of the proximal as well as distal end of the shunt depends upon septal wall height/ thickness. The increasing range of inner diameter of the shunt may be in range of 0.5-1.5 mm. The atrial septum height is in a range from 23-40 mm depends upon septal wall thickness and found in range of 0.5-2.0 mm. The thickness of the septal wall and width of struts in a ranges from 2-6 mm and 140-220 µm, respectively.

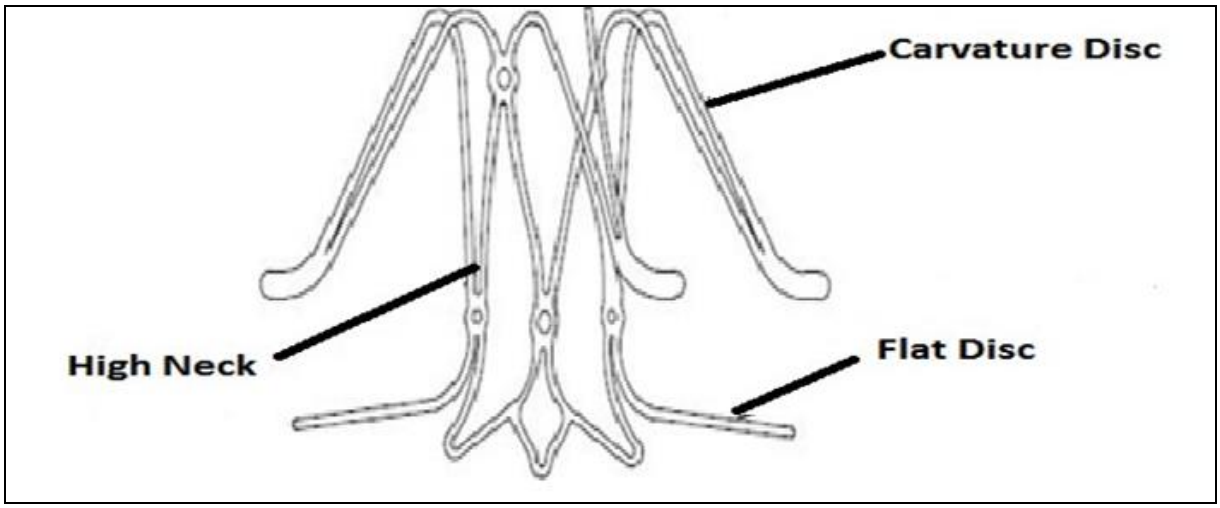

Fig 1: Flat Disc Shunt Implant

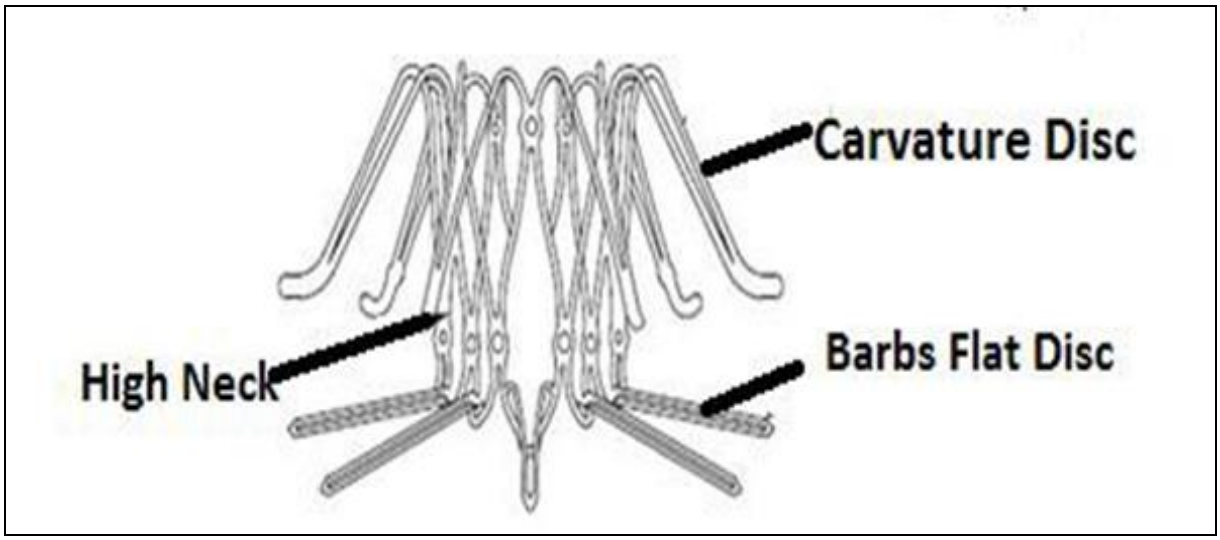

Fig 2: Barbs Flat Disc Shunt Implant

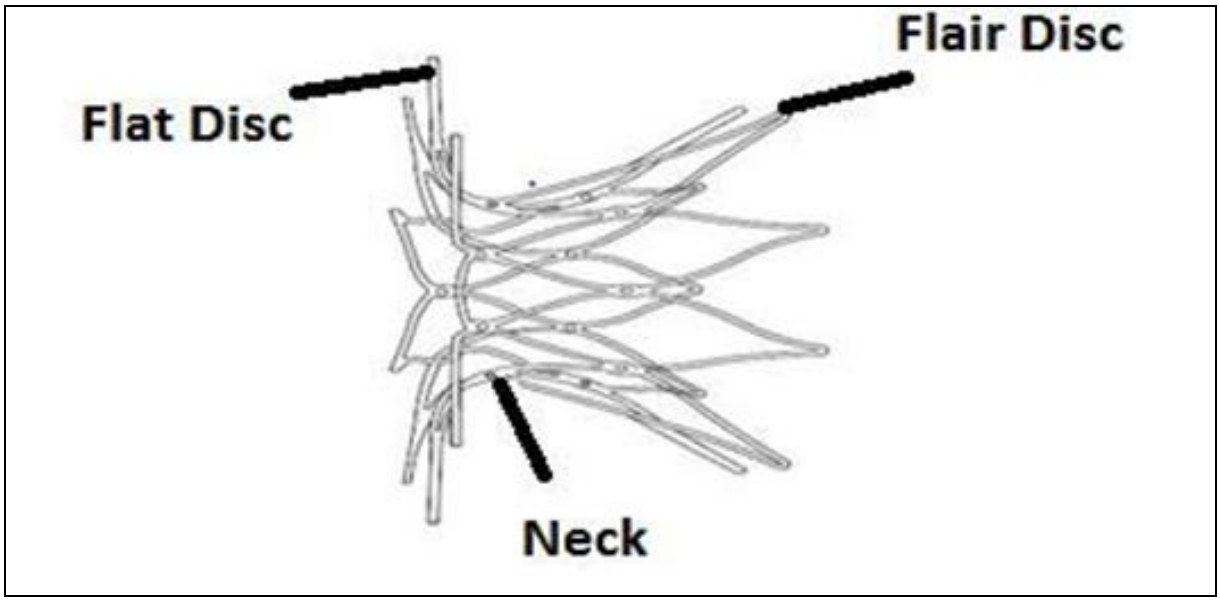

Fig 3: Flair Disc Shunt Implant

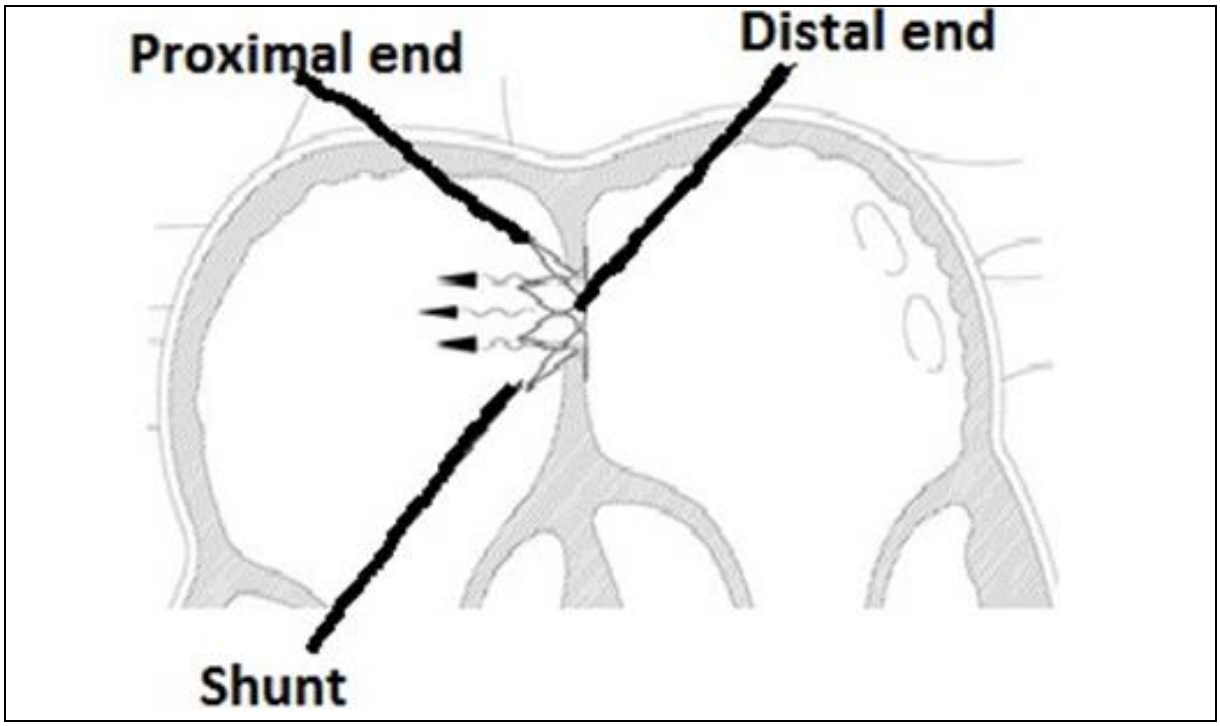

Fig 4: Implant of Shunt

The large cells were fabricated in shapes such as pear, petal, diamond, combat, and sigma, etc. The medium cell constitutes the neck portion of the frame. The medium and small cells were fabricated in shape such as diamond, petal, etc. The small cell constitutes the flat disc of the frame. The large, medium, small cells have length and width in the range of 10-15 mm and 0.5-1.0 mm, respectively. The end of the shunt includes an outer diameter. The outer diameter of the proximal end and distal end of the shunt were in a range of 15-21 mm. The neck portion at the intermediate region of the frame includes an inner diameter and a predefined length. The flat disc of the shunt was covered with a fabric. The fabric was attached by means of without limitation, shrink process or stitching. The fabric was selected from but not limited to Polytetrafluoroethylene (PTFE), Polyethylene terephthalate (PET) or any non degradable material. The tissue was attached to the proximal end of shunt by means of without limitation, suturing. The thickness of fabric and tissue is in a range of 80-200µ and 50-100µ, respectively. The distal end of the frame includes a plurality of barbs. The length and width of the barbs are in a range of 3-8 mm and 0.5-1.0 mm, respectively.

Table 1: shows an exemplary size range of the shunt as per the dimension of the atrial septum of the heart

Particulars	Size 1	Size 2	Size 3	Size 4
Atrial Septum Height (mm)	23-26	27-30	31-35	36-40
Shunt Height (mm)	6	8	10	12
Shunt Inner Diameter (mm)	6	7	8	9
Shunt Outer Diameter (mm)	15	17	19	21

Result and Discussion

The shunt creates a passage or vent between the left and right atrium to divert elevated blood flow from the left to right atrium in controlled manner to reduce the chances of diastolic heart failure. The shapes of the shunt have enhanced strength; provide adequate conformity to the septal wall of the heart which can be deployed at the treatment site with ease. The shapes of the shunt provide enhanced performance under low and high blood pressure at the left atrium by creating a passage for blood flow from the left to right atrium.

The blood flow from the left to the right atrium significantly reduces the excess blood pressure at the left atrium, thereby preventing detrimental consequences to the patient. The adequate shape and size of the shunt helps in reducing stress at an implantation site, confirm adequately to the septal wall which reduces chances of migration or deviation of the shunt at the implantation site. For loading the device smoothly in catheter, the shunt has low crimp profile.

The nitinol alloy is chosen due to its enhanced elasticity shape memory properties. The inclination helps to properly accommodate the shunt with the atrial septal wall of a patient. An appropriate size of the shunt as per the dimension of the atrial septal wall helps in controlled transfer of blood from the left to right atrium for achieving desired pressure in both upper chambers of the heart. The distal end of the shunt having more struts which provide more support at the septal wall leading to prevention of deviation and migration of the shunt. The height of the intermediate region was greater to maintain the passage of the septal wall for enough blood flow from the left to right atrium and also prevent deviation of the shunt from its place as well as to provide sufficient angle of inclination to the curvature disc which results in enhanced holding capacity of the shunt at the septal wall of a patient. The inclination of shunt helps to properly accommodate with the atrial septal wall of a patient. Higher length of the intermediate region leads to an enhanced decrease in blood pressure at the left atrium.

The flair disc at the proximal and the flat disc at the distal end of the frame help to accommodate the shunt at the septal wall which prevent migration/deviation of the shunt from its location. The shape of the shunt was easily loaded in the catheter may provide immediate reduction of blood pressure at the left atrium due to the flair disc and neck portion of the shunt. (Repeated few times)

The neck portion play a vital role in the treatment of the diastolic dysfunction. The adequate diameter of the neck portion plays a vital role in the treatment of the diastolic dysfunction. The adequate diameter of the neck portion is required to provide adequate blood flow from the left to right atrium, thereby achieving required blood pressure at the left atrium. The plurality of cavities should provided to accommodate radio opaque markers to enhance visualization of the shunt under fluoroscopy. The inclination angle between the flair disc and the flat disc helps to load the shunt smoothly into catheter as well as minimize jerking during deployment procedure. The curvature disc at proximal end of the frame help properly accommodate the shunt at the septal wall prevent migration of the shunt from the treatment site. It will well be accommodating with the atrial septal wall thickness as per patient's heart anatomy. The curvature disc at proximal end of the frame help to properly accommodate the shunt at the septal wall which prevent migration of the shunt from the treatment site.

The angles of the inclination helps to load the implant smoothly into the catheter as well as it minimize the jerking effect during deployment process. The barbs of the shunt provides spring back effect possess enhanced strength due to which the shunt can withstand rapid fluctuations of blood pressure. The barbs of the shunt include blunt edges that prevent penetration of the septal wall during deployment and placement of shunt. The flat disc of the shunt was covered with a fabric leading to faster tissue growth, prevention of deviation of the shunt from the site of implantation and enhanced adherence to the septal wall of the heart.

The e*x-vivo* study of interatrial shunt implant (IASI) conducted for evaluate the delivery procedure and to create shunt by deployment of inter atrial shunt implant in *ex vivo* porcine model. A number of observations were made during the deployment and afterward; The shunt/passage created by the implant was achieved successfully. The thickness of the implant could be increased to attain the desired results. The deployment mechanism used in the delivery system fulfills its intended purpose, although it could be modified to achieve more precise and accurate implantation. The implant is well placed and aligns with the atrial septal wall. The *ex-vivo* study of interatrial shunt in porcine model concluded that the delivery system and implant is use to create shunt by deployment procedure is satisfactorily working. The implant was successfully accommodated in the septal wall. The trans-

septal kit would be helpful for more accurate delivery and deployment procedure of shunt. Further, the design optimization of the implant would improve the required mechanical properties to well accomplish the intended use.

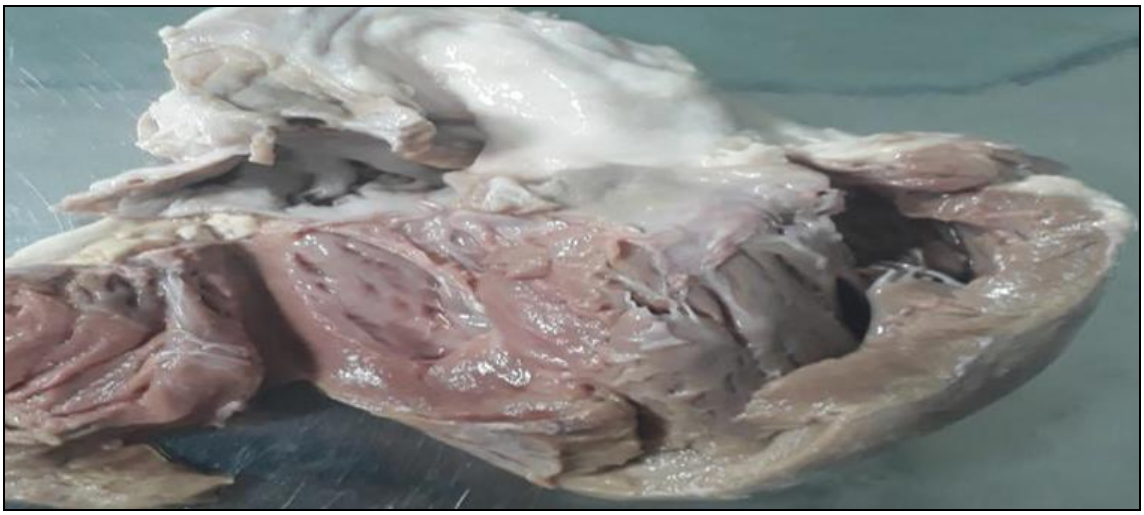

Fig 1: shows that the heart was dissected frontally to locate the inter atrial septal wall.

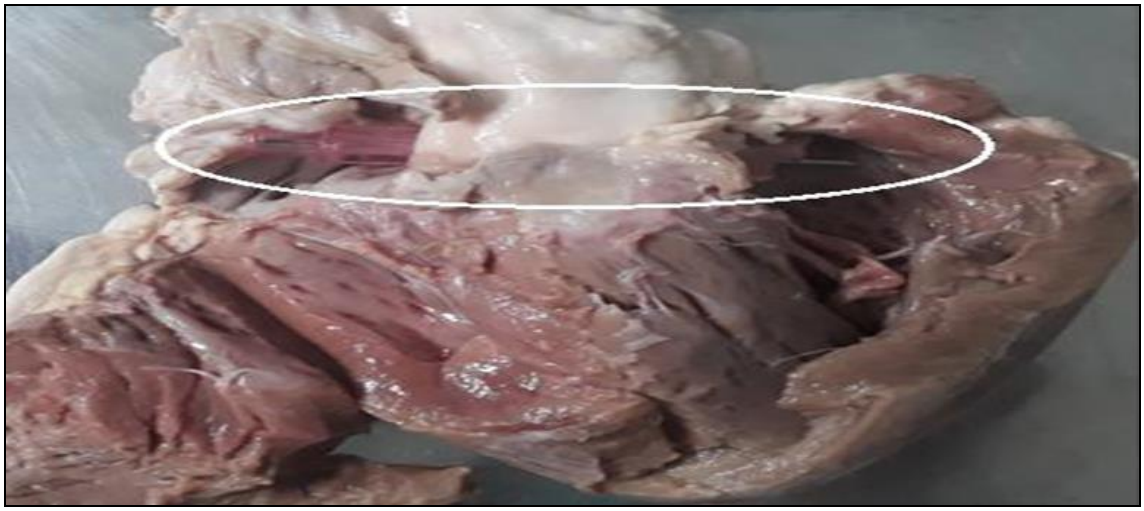

Fig 2: shows that the inter atrial septal wall was punctured using 16 gauge needle.

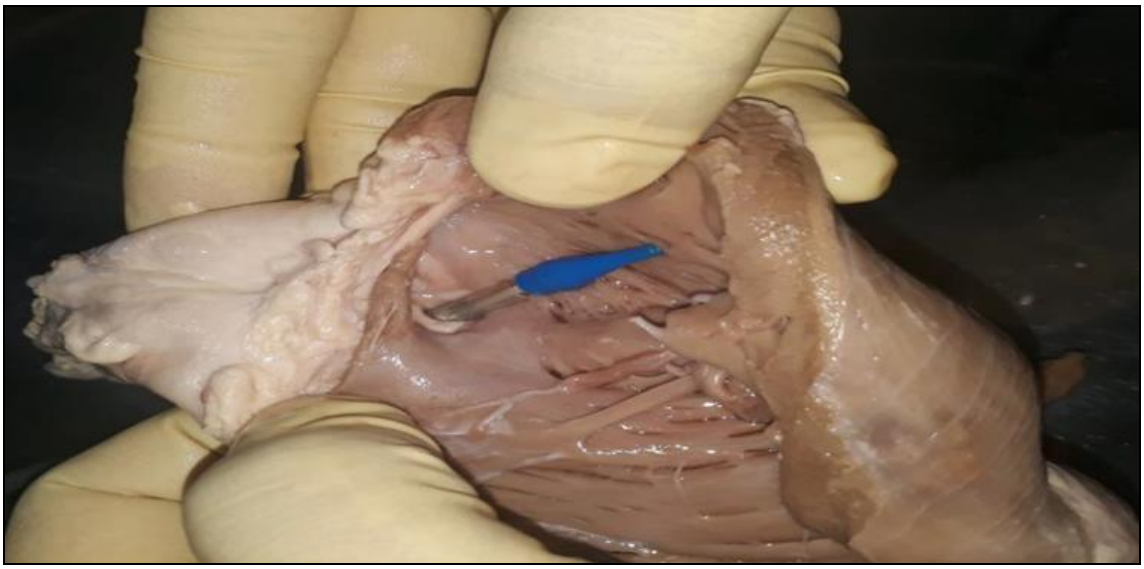

Fig 3: shows that the delivery system was passed through the septal wall using the hole created with the assistance of needle.

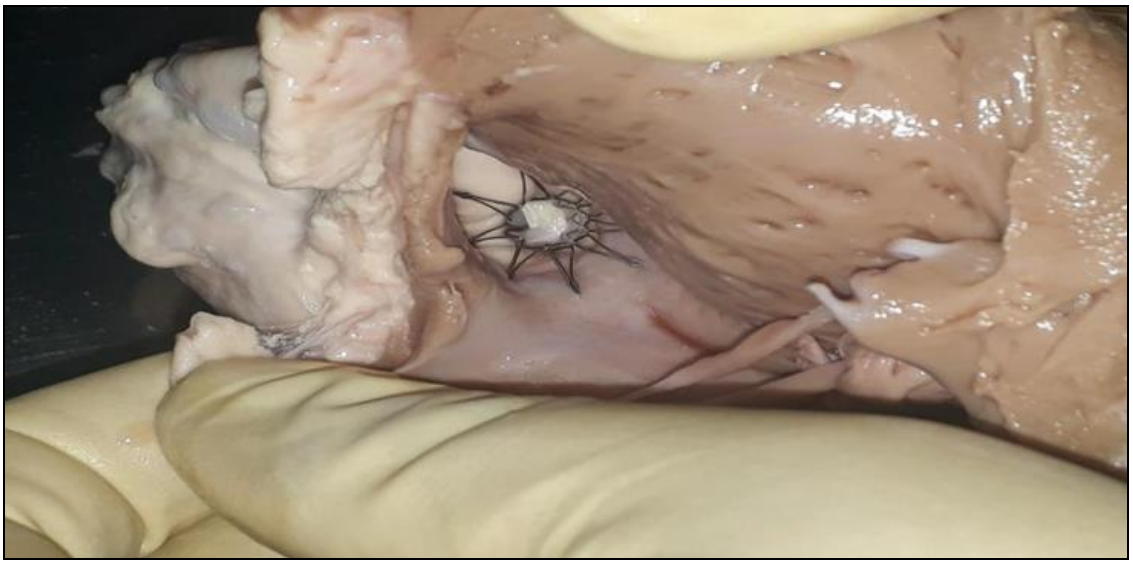

Fig 4: shows that the implant was deployed successfully at the atrial septal wall

Conclusion

The present research concluded that interatrial shunt devices represent a class of devices with a unique mechanism to directly reduce left atrial pressure, improve exercise tolerance, potentially improve clinical outcomes and prevent heart failure. The implant device with the goal allowing direct reduction in left atrial pressures through the creation of a left to right shunt. During e*x-vivo* study the implant was successfully accommodated with the septal wall and the delivery of the implant was smooth and easy to handle.

References

1. Pedra CAC, Pihkala J, Benson LN, Freedom RM, Nykanen D. Stent implantation to create interatrial communications in patients with complex congenital heart disease. Catheterization and Cardiovascular Interventions,1999:47(3):310-313.
2. Joseph J Cuthbert P, Pierpaolo Pellicori, Andrew L Clark. Interatrial shunt devices forheart failure with normal injection fraction: a technology update. Medical Devices: Evidence and Research,2017:10:123-132.
3. Sondergaard L, Reddy V, Kaye D, Malek F, Walton A. *et al*. Transcatheter treatment of heart failure with preserved or mildly reduced ejection fraction using a novel interatrial implant to lower left atrial pressure. European Journal of Heart Failure,2014:16(7):796-801.
4. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in prevalence and outcome of heart failure with preserved ejection fraction. N Engl J Med,2006:355:251-259.
5. Steinberg BA, Zhao X, Heidenreich PA, Peterson ED, Bhatt DL, Cannon CP, Hernandez AF, Fonarow GC. Trends in patients hospitalized with heart failure and preserved left ventricular ejection fraction:prevalence, therapies and outcomes. Circulation,2012:126:65-75.
6. Kaye D, Shah SJ, Borlaug BA, Gustafsson F, Komtebedde J, Kubo S, *et al*. Effect of an interatrial shunt on rest and exercise hemodynamics: results of a computer simulation in heart failure. J Card Fail,2014:20:212-221.
7. Webb G., and Gatzoulis M. A. Atrial septal defects in the adult: recent progress and overview. Circulation,2006:114:1645-1653.
8. Masura J, Gavora P, Podnar T. Long term outcome of transcatheter secundun type atrial septal defect closure using amplatzer septal occluders. J Am Coll Cardiol,2005:45:505-507.
9. Trigo MD, Bergeron S, Mathieu B, *et al*. Unidirectional left to right interatrial shunting for treatment of patients with heart failure with reduced ejection fraction: a safety and proof of principle cohort study. The Lancet,2016:387(10025):1290-1297.
10. Shah SJ, Borlaug BA, Chung ES, Cutlip DE, debonnaire P. *et al*. Atrial shunt device for heart failure with preserved and mildly reduced ejection fraction (REDUCE LAP - HF II): a randomised, multicentre, blinded, sham controlled trail. The Lancet,2022:399(10330):1130-1140.
11. Rodriguez RC, Burkhoff D, Latib A, Granada JF. A Glimpse into the future of Transcatheter Interventional Herat failure Therapies. JACC: Basic to Translational Science,2022:7(2):181-191.
12. Emani S, Burkhoff D, Lilly SM. interatrial shunt device for the treatment of heart failure. Trends in Cardiovascular Medicine,2021:31(7):427-432.
13. Smeenk FWJM, Postmus PE. interatrial right to left shunting developing after pulmonary resection in the absence of elevated right sided heart pressure: Review of the Literature. Chest,1993:103(2):528-531.
14. Cuthbert JJ, Pellicori P, Clark AL. interatrial shunt device for heart failure with normal ejection fraction: a technology update. Med Devices (Auckl),2017:10:123-132.

15. Thomas JD, Tabakin BS, Ittleman FP. Atrial septal defect with right to left shunt despite normal pulmonary artery pressure. J Am Coll Cardiol,1987:9(1):221-224.
16. Lilly SM, Burkhoff D. Technologies for treating left atrial decompression in heart failure. Cardiac Interventions,2018:12(1):59-61.
17. Nassif M, Berto MA, Bouma BJ, Straver B, Blom NA, Koch KT, *et al*. Historical developments of atrial septal defect closure devices: what we learn form the past. Expert Review of Medical Devices,2016:13(6): 555-568.
18. Albada MEV, Schoemaker RG, Kemna MS, Cromme Dijkhuis AH, Vaghel RV, Berger RMF. The role of increased pulmonary blood flow in pulmonary arterial hypertension. European Respiratory Journal,2005:26:487-493.
19. Obokata M, Reddy YNV, Shah SJ, Kaye DM. *et al*. Effects of interatrial pulmonary vascular function in heart failure with preserved ejection fraction. Journal of the American College of Cardiology,2019:74(21):2539-2550.
20. Lehner A, Schulze Neick I, Fischer M, Fernandez Rodriguez S, Ulrich S, Haas NA, Jakob A. The creation of an interatrial right to left shunt in patients with severe, irreversible pulmonary hypertension: Rationale, Devices, Outcomes. Current Cardiology Reports, 2019.
21. Behnke IM, Akintuerk H, Thul J, Bauer J, Hagel KJ, Schranz D. Stent implantation in the ductus arteriosus for pulmonary blood supply in congenital heart disease. Catheterization and cardiovascular Interventions,2004:61(2):242-252.
22. Knepp MD, Rocchini AP, Lloyd TR, Aiyagari RM. Long term follow up for secundum Atrial septal defect closure with the amplatzer septal occluder. Congenital Heart Disease,2010:5(1):32-37.
23. Shi D, Kang Y, Zhang G, Gao C, Lu W, Zou H, Jiang H. Biodegradable atrial septal defect occluders: A current review. Acta Biomaterialia,2019:96(15):68-80.
24. Emani S, Burkhoff D, Lilly SM. Interatrial shunt devices for the treatment of heart failure. Trends in Cardiovascular Medicine,2021:31(7):427-432.