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PROJECT COMPLETION REPORT

Project Number : P 8179

Title of the Project : Development of novel prototype mechanical clot retriever for the treatment of acute cerebral ischemic stroke

Funding Agency Name : DBT

Project Reference Number provided by the Funding Agency:

BT/PR14604/MED/32/410/2015

Principal Investigator (Name & Address) :

Dr Santhosh Kumar K, Dept of Imaging Sciences and Interventional Radiology,
SCTIMST

Co-Investigators (Name & Address):

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Implementing Institution : SCTIMST

Collaborating Institutions : Nil

Date of Commencement : 12/2/2018

Duration : 3 years

Date of Completion : 30/06/2021

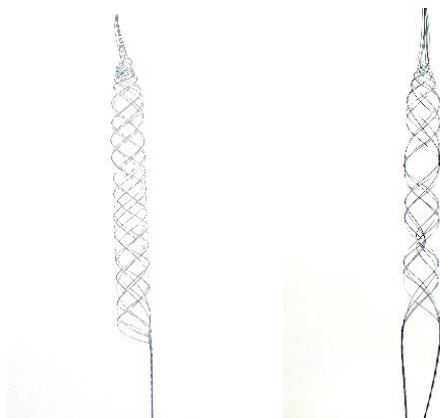
Objectives as approved :

1. Development of prototype nitinol-based stent retriever
2. Interaction of clot with newly developed prototype

Deviation made from original objectives if any, while implementing the project and reasons thereof :Nil

Field/Experimental work giving full details of summary of methods adopted, data collected supported by necessary tables, charts, diagrams and photographs :

1. Specification Development for stentriever based on clinical need and relevant international standards.
2. CAD modelling of the device using computer aided design tools.
3. Selection of material wire, sourcing and qualification.
4. Prototyping and manufacturing of device.
5. Patenting and Patent filing
6. Assessing mechanical properties using finite element model.
7. Process developed for mounting the device on delivery system.
8. Delivery system working prototype developed.
9. Invitro test models developed
10. Invitro testing of device which includes deployability, dimensions, clot interactions.



Detailed analysis of results :

The braided stent retriever has a braided structure which will ideally provide variable cell strut construct. Variable strut construct facilitates better clot interaction and entrapment. A braided distal basket using Nitinol wires would prevent distal embolization.

SCTIMST has already developed its own in-house braiding technology and have already has the expertise of braiding with its ongoing projects which includes, flow diverter stents and atrial septal defect occluder. SCTIMST already had acquired the nitinol wires of various diameters. The radial strength of the braided stent retriever is being studied both using finite element analysis and other invitro testing techniques.

Thus, the braided stent retriever provides an easier and simpler alternative without having to compromise on the aforementioned design features. The design provided a variable strut construct and simpler distal basket utilizing the existing facilities at the institute.

Two novel concepts of braided stent retrievers were developed. The braided stent retriever consists of a braided distal basket, two planar tails and a braided clot interacting body. The braided distal basket will help in the prevention of distal embolization. The two planar tails would help in easy re-sheathing of the stent retriever.

The two designs are different in terms of the clot interacting body. In one of the concept, a continuous 1x1 diamond braid was employed for the whole length (Figure 3 (a)). In the second design a segmented body was created using 1x1 diamond braided unit cells separated by 2 planar braids (Figure 3 (b)). The second design would ideally provide better conformability to complex neurovasculature. The performance of the two concepts is tested in-vitro as mentioned later in the report.

The two braided concepts have been prototyped (Figure 3) inhouse using the existing wires and technology. Several samples had to be generated to finalize the procedure for each of the two concepts. The braiding is performed over a mandrel which once braided is heat treated to shape set the nitinol wires. Samples also varied in the diameter of the wire used to produce the stent retrievers. A total of 34 samples have been produced till date which involves a variation of the two braided concepts and 3 different diameter wires (80um, 100um, 150um).

The pusher wire is used from predicate devices. It needs to be made from a tapered wire of 0.5mm diameter and tapering down to about 200 microns distally. This wire is then attached to the proximal part of the clot retriever having the planar braid using a hypotube and medical grade adhesive. The hypotube is made of polyimide and has an ID of 0.5mm and OD of 0.6mm

**Summary sheet of not more than 2 pages under following heads :
(Title, Introduction, Rationale, Objectives, Methodology, Results, Translational Potential)**

Attached

Contributions made towards increasing the state of knowledge in the subject :

Our work showed that the prototype of stent retriever for the purpose of mechanical clot removal from the arteries could be made using braided stents. It retained radial dimensions and displayed no elongation of the stent while or after retrieval, which are useful properties that enable successful clot capture.

Conclusions summarising the achievements and indication of scope for future work :

Future work should include studying the consistency of dimensions of devices of various diameters, performance difference of stents with differing nitinol diameters, its effect on clot retrievability and interaction in physiological milieu. A future study developing the device with intent of in vivo use and transfer of technology could be envisaged.

Science and Technology benefits accrued :

a. List of research publications with complete details :

Applied - Indian Patent Application No: 201941022802 dtd 08/06/2019 titled "A Braided Stent"

b. Manpower trained on the project :

Research Scientists or Research Fellows : 1

No. of PhD's produced : Nil

Other Technical Personnel trained : Nil

c. Patents taken, if any : 1

d. Products developed, if any : Prototype of nitinol based stent retriever

20. Abstract: (In 300 words for possible publication in Bulletin)

a. Background:

b. Materials:

c. Results:

d. Conclusion:

21. Procurement/Usage of Equipment: Nil

a. Details of Equipment: NA

Sl. No.	Name of Equipment	Make/ Model	Cost (Rs.)	Date of Installation	Utilisation	Remarks regarding maintenance breakdown

b. Suggestions for disposal of equipment(s):

Dr.Santhosh Kumar K
25.10.2023

(Name and Signature of PIs with date)

Routing: Signed copy of "Project completion Report" by PI → root@sctimst.ac.in, rpc@sctimst.ac.in

Development of novel prototype mechanical clot retriever for the treatment of acute cerebral ischemic stroke.

Introduction and rationale

Retrievable stents were serendipitously found to be useful in the retrieval of clots and initial report of its use in acute stroke demonstrated promising results. Further on, several large series and registry results confirmed excellent recanalization rates compared to existing modalities of treatment. Following two noninferiority trials (Trevo 2, SWIFT) comparing its efficacy to the existing standard of therapy MERCI mechanical clot retrieval clearly showed superior efficacy of these devices and has since been incorporated in routine stroke therapy.

The recent randomised studies (MR Clean, Escape trial, Extend Ia, Swift Prime) demonstrated clear benefit of mechanical interventions in terms of clinical outcomes, morbidity and mortality with acceptable safety profile. Following these trials, standard of care in acute stroke has shifted to emergent mechanical clot removal if patient presents within the therapeutic window period.

In our country, we face unique challenges as far as treatment of these devastating diseases are concerned 1) Disease is increasingly common affecting younger population causing huge financial and social burden. 2) Treatment is expensive and unaffordable for vast majority of population 3) The stroke due to cardiac and valvular disease is common and the performance of present devices in such situations is uncertain (based on our clinical experience)

Hence, development of indigenous device aiming better clot interaction and cost reduction is essential.

Objectives

1. Development of prototype nitinol-based stent retriever
2. Interaction of clot with newly developed prototype

Materials and Methodology

Taking into consideration, the properties of Nitinol and the drawbacks of the existing devices, a list of ideal design features were identified. The following are the proposed design features:

1. Possess optimal radial strength.
2. Provide distal baskets to prevent distal embolization.
3. Variable cell strut construct.
4. Design for manufacturability.

The Braided stent retriever has been discussed in detail in this report. The design offers good radial strength and variable cell strut construct along with a distal basket. Radial strength is critical in piercing through the clot, whereas, variable cell strut construct would help in better clot interaction.

Creo (M/s PTC, USA) was used as a CAD tool in creating the model of these designs for the purpose of finite element analysis. In our case, finite element analysis is aimed at performing a crimping

analysis of the stent which would also help in predicting the radial strength of these devices. Finite element analysis invariably involves several assumptions and approximations. Especially with the braided design there are several limitations in achieving convergence of the finite element model.

The Braided clot retriever requires nitinol wire braiding. The braided clot retriever has three major components to itself. The body of the stent which interacts with the clot and helps in trapping the clot. The distal basket prevents distal embolization and the planar braided tails help in easy retraction of the stent into the catheter.

Results

The following design has been applied for an Indian patent -

Braided Stent Retriever:

The braided stent retriever has a braided structure which will ideally provide variable cell strut construct. Variable strut construct facilitates better clot interaction and entrapment. A braided distal basket using Nitinol wires would prevent distal embolization.

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Thus, the braided stent retriever provides an easier and simpler alternative without having to compromise on the aforementioned design features. The design provided a variable strut construct and simpler distal basket utilizing the existing facilities at the institute.

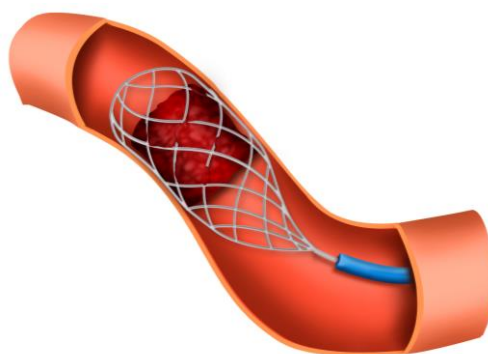


Figure 2: A representative figure of mechanical clot retrieval using Braided Stent Retriever

Two novel concepts of braided stent retrievers were developed. The braided stent retriever consists of a braided distal basket, two planar tails and a braided clot interacting body. The braided distal basket will help in the prevention of distal embolization. The two planar tails would help in easy re-sheathing of the stent retriever.

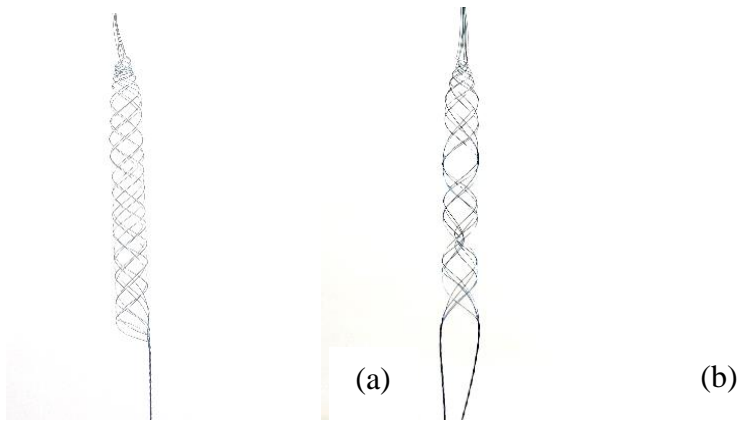


Fig 3: (a) Concept-1 Prototype (b) Concept-2 Prototype

The two designs are different in terms of the clot interacting body. In one of the concept, a continuous 1x1 diamond braid was employed for the whole length (Figure 3 (a)). In the second design a segmented body was created using 1x1 diamond braided unit cells separated by 2 planar braids (Figure 3 (b)). The second design would ideally provide better conformability to complex neurovasculature. The performance of the two concepts is tested in-vitro as mentioned later in the report.

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Discussion

The project was aimed at developing a braided model, so the study is currently being focused on the braided stent. Currently, design specifications and braiding procedure for the two braided stent retriever concepts have been finalized. FEA (Figure 4) of the same has been performed to study the crimpability and radial strength characteristics.

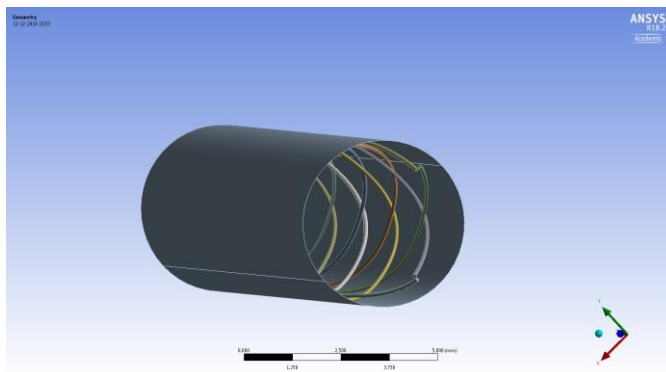


Figure 4: FEA crimping setup for the braided structure using a hyper-elastic outer crimping surface. Simultaneously, the patenting work was completed for the before mentioned braided stent retriever concepts. A provisional as well as complete patent has been filed with DBT as a co-applicant at the Indian Patent office.

Several pre-clinical invitro testing procedures have been identified to test the performance of the prototypes according to FDA standards [1]. The following are the tests to be performed

- (1) The patient contacting components of the device must be suitable for blood contacting use.
 - (2) In-vitro performance testing must demonstrate that the device performs as intended under anticipated conditions of use, including:
 - (i) Mechanical testing to demonstrate the device can withstand anticipated tensile, torsional, and compressive forces.
 - (ii) Mechanical testing to evaluate the radial forces exerted by the device.
 - (iii) In-vitro testing to verify the dimensions of the device.
 - (iv) In-vitro testing must demonstrate the device can be delivered to the target location in the neuro-vasculature and retrieve simulated thrombus under simulated use conditions.
 - (v) In-vitro testing must evaluate the coating integrity and particulates under simulated use conditions.
 - (3) Performance data must support the sterility and pyrogenicity of the patient contacting components of the device.
 - (4) Performance data must support the shelf-life of the device by demonstrating continued sterility, package integrity, and device functionality over the specified shelf-life.
- In-vitro tests 2(i), 2(iii), and 2(iv) have been performed on the prototypes.

In order to perform the delivery and clot interaction studies an acrylic model as described below was developed. At the same time, a silicone model and thrombus simulants have been sourced in order to perform the tests. The silicone models have been integrated in an acrylic box in-house.

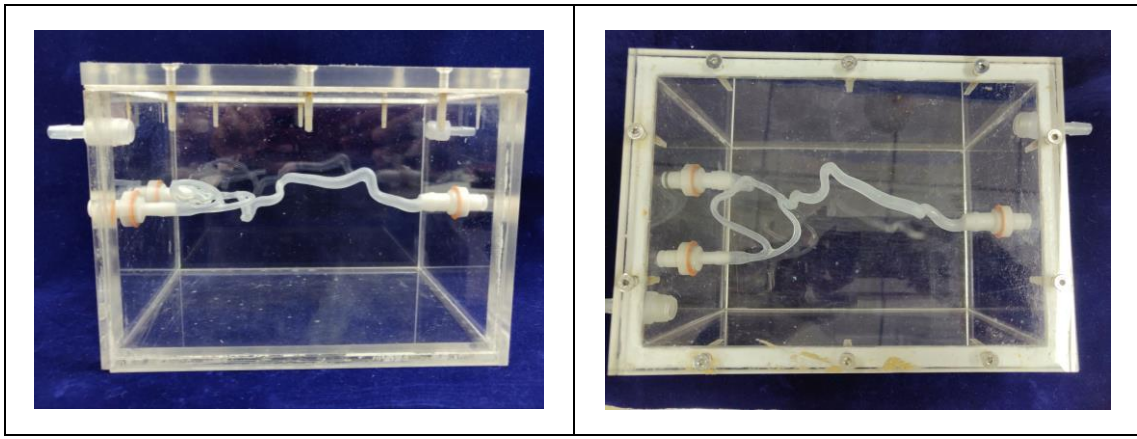


Figure 5: Acrylic neuro-vascular test setup

Experiments performed.

Two prototypes of braided stent: prototype 1 and 2 were attached with a 200 microns diameter and 200 mm length. The stents were introduced into a microcatheter of 0.27 inch ID. An experimental set up as shown into figure 5 was created and the thrombus stimulant was introduced into the tube. The experiments were conducted in both flowing and static situations. The microcatheter was crossed beyond the clot stimulant and the stent was deployed by unsheathing. The stent of both the designs were seen to expand uniformly. After a dwell time of 3-5 minutes the stent was retrieved, and while retrieving the stent was seen to capture the clot. The clot was retrieved without fragmentation of distal migration under flowing condition. On inspection from outside, the clot was seen to be adherent to the stent filaments, which was probably enabling the stent to retrieve the clot. There was no elongation of stent while removal. It maintained its radial diameter and radial force after retrieval.

The experiment was conducted with an available clot retriever (Trevor provue) and this stent too demonstrated clot retrieval. However the diameter of the stent was smaller on inspection and it didn't automatically expand to its original radial diameter. A few representative pictures are shown in Figure 6



Figure 6: Expanded stents, deployed across clot

Translational potential

Our work showed that the prototype of stent retriever for the purpose of mechanical clot removal from the arteries could be made using braided stents. It retained radial dimensions and displayed no elongation of the stent while or after retrieval, which are useful properties that enable successful clot capture.

Future work should include studying the consistency of dimensions of devices of various diameters, performance difference of stents with differing nitinol diameters, its effect on clot retrievability and interaction in physiological milieu. A future study developing the device with intent of in vivo use and transfer of technology could be envisaged.

Important Instructions:

STPR must be complete in all respect. All the information needs to be compulsorily provided, otherwise STPR will be treated as incomplete and will not be evaluated or considered further. In case of 'Nil' / 'Not Applicable' information, the same may please be indicated.

In case of multicentric network project, combined Scientific and Technical Progress Report (STPR) requires to be submitted incorporating the progress of all components. The Project Co-coordinator/ PI will be responsible for this.

*Please indicate the reporting period [i.e. 1st year (I) / 2nd year (II) / 3rd year (III) / Completion Report etc.]. In case of completion report, please indicate that it is the 'Project Completion Report'.

Submission of STPR is linked with further continuation of the project, release of grant and final settlement of accounts.

STPR need to be submitted by post (5 copies+ soft copy in CD) and also by email in pdf file.
