Simulation of the Human Inferior Vena Cava
for
Evaluating IVC Interruption Devices

by

Martin Raymond Prince

Submitted in Partial Fulfillment
of the Requirements for the
Degree of
Bachelor of Science

at the
Massachusetts Institute of Technology
June 1980

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Abstract

A test apparatus for evaluating inferior vena cava (IVC) interruption devices has been built and made operational. It is designed to simulate venous flows, pressures, and temperatures that are in the realm of human experience. Various sizes of cellulose dialyzer tubing are used to model varying sizes of cava and a system of mirrors permits filming three views of device performance inside the apparatus. It has been used extensively to study and develop a unique new IVC interruption device, the Nitinol Filter, which is inserted into the body, without surgery, through a fine plastic tube (catheter) and converts into a blood clot filter by virtue of the thermal shape-memory phenomenon.

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II. Introduction

Clinical Aspects. 630,000 Americans are estimated to suffer significant health problems when large clots that form in their legs, break loose, and migrate to the lungs. For 200,000 Americans these clots, called pulmonary emboli, will be fatal (1). Pulmonary emboli block the flow of blood into the lungs and seriously compromise pulmonary function. At present, there are no good medical techniques for treating people who are diagnosed as being threatened by a pulmonary embolus. The standard treatment, anticoagulation therapy, allows significant emboli to migrate to the lungs in 7% of treated patients (2). A common surgical technique that prevents blood clots in the lower body from reaching the lungs by mechanically interrupting (see figure 1) the largest of veins leading from the legs to the lungs (IVC) has a 14% operative mortality rate (3). Two experimental devices, the Greenfield Filter and Mobin-Uddin Umbrella (figure 1), also mechanically interrupt the IVC, but with a less traumatic surgical procedure (4-6). These mechanical techniques for preventing pulmonary embolism by "filtering" blood flow in the IVC appear to be effective in capturing clots, as less than 3% of patients treated this way are reported to suffer from pulmonary embolism after placement of the interrupting device (3,7,8). However, there have been many reported cases of filter migrations and surgical complications (9-12). Clearly a technique which is both safe and effective for treating the
Figure 1a. Surgical techniques for interrupting the IVC

The clips, named after their inventors, fit around the outside of the vena cava to divide it into small or narrow channels.

Figure 1b. IVC interruption devices that fit inside the IVC
Patient threatened by pulmonary embolism is needed.

**Nitinol Blood Clot Filter** Such a device is being developed by Drs. Morris Simon and Aubrey Palestrant at Beth Israel Hospital (13). It is designed to mechanically interrupt the IVC but can be introduced into the body through a tiny plastic tube (catheter). The plastic tube is inserted into a vein in the groin, arm, or neck with a simple needle puncture which requires no surgery. This same tube is used for injecting radio-opaque dyes into the circulatory system as a diagnostic procedure to determine if a patient has had or is threatened by a pulmonary embolus. Therefore, delivery of the filter would be a simple extension of the diagnostic procedure, not an additional surgical procedure.

**Nitinol's Metallurgical Properties** This new filter concept is possible because of a special property of Nitinol, the alloy from which the filter is made, that was first described by W. J. Buehler in 1962 (14). At low temperatures, Nitinol forms a martensitic crystallographic structure which is quite malleable within a limit of about 8% strain. But when heated to higher temperatures (e.g. body temperature), Nitinol assumes any desired three-dimensional rigid shape which can be pre-assigned as desired (within the 8% strain limit)(15). So in this application, at room temperature the Nitinol blood clot filter is shaped into a straight wire. As a straight wire, the filter is passed
through the catheter and into the inferior vena cava. Once in
the cava, the wire comes into contact with blood at body
temperature and immediately assumes its high temperature,
pre-imposed filter shape. In this way, practically any filter
shape can be located in the inferior vena cava with minimal
risk, or discomfort to the patient.

**Nitinol Filter Development.** The key to developing this
device is optimizing the filter configuration for maximum
patient safety and clot capture effectiveness. This optimal
configuration has been achieved for animal sized filters and
over 40 Nitinol filters have been successfully delivered to
dogs. Nitinol Filter research is now focusing on optimizing
the filter configuration for the larger, human sized cava.
Because animals are expensive & inconvenient to work with,
have the wrong size cava, which cannot be easily examined
anyway (since animal tissues are not transparent), and for
humanitarian reasons, it is not possible to use animals for
comprehensively testing the mechanical properties of these
filters.
III. Goal of Present Study

This project is aimed at developing an appropriate test apparatus for evaluating human sized blood clot filters. It will encompass development of the testing apparatus, testing preliminary Nitinol Filter designs, and testing the Mobin-Uddin and Greenfield filters. This approach provides a basis for comparing the performance of Nitinol designs with filters currently being used in humans.
IV. Previous Work

Two in vitro test systems have previously been developed to test filters designed for dog sized cava. These early attempts were developed through the collaboration of Dr. Morris Simon at Beth Israel Hospital and Itzhak Bentov, an engineer/inventor in Wayland, MA. They provided this project with an invaluable experience in vena cava simulation.

The first design (figure 2) was simply a piece of Penrose latex tubing hooked up to a pump submerged in a temperature bath and fitted with ports to accommodate the delivery catheter and experimental emboli. Visualization was made by X-ray fluoroscopy with cine documentation. The system provided only one view of filter performance and involved the inconvenience of using fluoroscopy.

The second system (figure 3) was substantially improved by simulating the cava with transparent plastic tubing (instead of radiolucent latex tubing) which permitted filter visualization and documentation without X-rays. Two mirrors were strategically oriented around the "cava" to permit filming three projections of filters inside the transparent cava. It was substantially iterated to provide monitoring and control of temperature, pressure, and flow. Also added was a lens to magnify the projection of the end-on view (looking down the axis of the cava). The optics worked well but the system had several shortcomings. Being an open system, it was impossible to simulate filter pressure gradients observed to occur in animals when a large clot occluded the filter. There
Figure 2. First test system

- PUMP
- 35mm cine camera
- X-RAY DETECTOR
- TEMPERATURE BATH
- Blood clot delivery port
- Filter test section
- Filter delivery port
- X-RAY EMITTER
Figure 3. Second test system
was a poor correlation between filter clot capture ability in vitro as compared with animal studies using identical clot. It is postulated that in animals, clots are initially captured by the filter and then forced through as pressure builds up behind the clot. In animals there is also a water hammer effect due to pulsatile venous blood flow which was not simulated in this early apparatus. The vertical orientation of the apparatus affected clot flow (since the specific gravity of clot \( > 1 \)) and made filter deliveries awkward and unphysiological. Patients always lay horizontal during this type of procedure. Perhaps the greatest deficiency was the simulated caval tubing which came in one size suitable only for modeling dog cavae. It was also made of a rigid plastic tubing which poorly simulated the properties of real caval membrane.
III. Test Apparatus Design

Blood clot filters have three basic qualities that must be tested: biocompatibility, deliverability, and effectiveness in capturing clot. Nitinol biocompatibility has been and will continue to be studied in animals (16-18) so the test apparatus will focus primarily on evaluating filter deliverability and clot capture effectiveness. To test these qualities the test apparatus must:

1. be transparent so investigators can see what's happening
2. have ports for delivering clots and filters
3. simulate inferior vena cava physiology as closely as possible

In generating a test apparatus design, the dog filter testing apparatus was carefully examined and the best qualities of this previous apparatus were incorporated into the new design.
The Design

Figures 4, 5, & 6 show diagrams of the test apparatus hydraulics, optics, and the total system.

Inferior Vena Cava. The cava is simulated by cellulose dialyzer tubing. This tubing is transparent, thin, pliable, and easily torn so that traumatic filter deliveries are very obvious. It does not have as much elasticity or as many branching vessels as the human IVC but these are considered to be minor shortcomings. Vessel diameters of 15mm, 19mm, & 28mm have been obtained from Fischer Scientific and used on the test apparatus. (It is believed that other suppliers will be able to provide additional cava sizes in the appropriate range.) A water chamber surrounding the artificial cava provides structural support without interfering with cava function. By having flat surfaces, this chamber also eliminated the optical distortions associated with looking into the curved surface of the simulated cava. Since computerized axial tomographs show the vena cava to be oval in cross section, a disk with an oval hole has been designed to hold the simulated vena cava in an oval cross section at the upstream end of the test chamber. Recent computerized axial tomographs have shown that the vena cava is oval in cross section.

Physiologic Controls. Temperature is monitored downstream from the test section using a copper/constantan
Figure 4. Test apparatus hydraulics
Optics

Figure 5. Test apparatus optics

Another light and diffuser are behind the test chamber.
Figure 6. The total system with a filter in the test chamber
thermocouple with a digital display that is recorded on film along with the three vena cava projections. The thermocouple leads are 0.005 inches in diameter and respond nearly instantaneously to subtle changes in temperature and measure to an accuracy of 0.2 C. Temperature is maintained at 37 C with a 17 liter (high thermal capacitance), open temperature bath. The test fluid is water which has the advantages of being transparent, clean, cheap, and easy to use. Its flow is controlled by a variable speed pump and a Wallace & Tiernan float type flow meter/regulator that operate in tandem through a range of 0 - 10 liters/minute. Pressure is monitored upstream of the test section with a diaphragm pressure meter accurate to within 1mm Hg (13mm water). The system is sealed, but is connected to an open-ended tube which can be varied in height to set the maximum pressure gradient allowed across the filter. Turbulence is assessed by introducing a ribbon of blue dye through an eight inch long, 23 gauge needle with its tip located just upstream from the filter. The amount of dye dispersal beyond the filter provides a qualitative estimate of filter generated turbulence.

**Filter Removal** Test chamber components slide along a bracket to allow quick disassembly for easy removal of test filters, clot, or cellulose tubing. A pressurized air outlet is attached to the hydraulics to flush out test fluid just prior to opening the chamber so that nothing spills.
Documentation Events in the test chamber are recorded on 16mm movie film by an Arriflex S movie camera. Mirrors present three projections (front, side, & end-on) of the simulated cava while a mask frames the three views and hides the guts of the device from the camera to improve movie aesthetics. Film speed can be varied and is optimized by trading off film cost with resolution. Filter deliveries are run at 24 feet/minute while blood clot studies are filmed at 36 feet/minute for higher resolution.
VI. Experimental Procedure

This apparatus has been used to conduct two series of experiments, one geared to Nitinol Filter development, another geared toward evaluating the Mobin-Uddin Umbrella and the Greenfield Filter. For both experimental series the system was prepared in identical ways. First the temperature bath was filled with 17 liters of non-aerated distilled water and set to maintain 37.0°C. Cellulose tubing was fitted in the test chamber by feeding it through the oval slot and stretching each end over the chamber seals. For cava smaller than 25mm, special adaptors were used to avoid ripping the cellulose tubing. The test chamber was then snapped into the test system and sealed by tightening two bolts. Flow was turned on and calibrated by diverting the caval flow to a two liter graduated cylinder for 10 seconds. Air in the test chamber was removed by opening a strategically located valve. Camera settings and mask position were checked to insure proper documentation and the scheduled experiment of delivering a filter, clot, or both was carried out. If clot was delivered, 150 ml of NaCl was added to the water bath to prevent osmotic pressure lysis of red blood cells in the clot. To remove the test chamber, the water flow was turned off, a pressurized air valve opened to flush water out of the system, and within 60 seconds, the chamber could be easily unbolted and removed. Once the chamber was free, filters inside it could be carefully examined and then removed with forceps. Usually many experiments were conducted in series so that much of the
preparation, i.e. loading the water tank, was done only once for each day of experiments. Typically setting up the system required 30 minutes and each experiment another 5 to 10 minutes.

**Nitinol Filter Development** Eleven variations on the Nitinol Filter were delivered over forty times using a variety of filter delivery systems and filter loading techniques. In all instances, the filters were delivered through a French 8 catheter and in some cases 3 - 5mm diameter clots challenged the filter. Typically, after a few deliveries of any one filter, several ways of improving the design would become apparent and the filter would be modified to reflect this improved understanding of filter performance.

**Clot Capture Studies** The second series of experiments involved challenging the Greenfield, Mobin-Uddin, and Nitinol filters with blood clot. Experimental clot was made by allowing dog blood to sit stagnant in tubing with a lumen 25% larger than the desired clot diameter. The clot was then sized into even lengths for delivery to filters in the test chamber. The system fluid (water) was primed with saline to prevent osmotic pressure lysis of red blood cells in the clot. All three filters were challenged with 5mm diameter clots 5mm long. The Nitinol and Greenfield filters were further challenged with 3mm diameter clots 5 - 10 cm long. In all experiments several clots were delivered in succession to the
filters before any were removed and all studies used 28mm diameter tubing.
VII. Results

**Nitinol Filter Development.** With the early designs many problems were quickly discovered relating to scratching the wall of the cava during delivery, not conforming to the cava size, orienting improperly, not anchoring to the caval wall, and more. Four of these Nitinol Filter prototypes are shown in figures 7, 8, 9, & 10. With each successive modification these problems and others have been substantially reduced so that the latest designs appear nearly mechanically acceptable for clinical application. Some of the early designs were not particularly effective in capturing clot but the latest designs seem to be at least as effective as the Greenfield Filter. At this point clot capture data for the Nitinol Filter are not statistically significant because only a few studies have been made with any one specific design. It is significant, however, that slow motion analysis of the films shows the exact mechanism of how clots are captured or how they pass through a particular filter design.

**Mobin-Uddin Umbrella.** This filter had to be positioned in the test chamber by hand because it was much too large to fit through the filter delivery port. It was even difficult to insert by hand because the desired orientation was unstable as shown in figure 11. Notice that in the stable configuration not all of the hooks engage the wall of the cava. It has been suggested that this is the cause of several Mobin-Uddin
Figure 7. Filter Delivery

Front and side view of the most recent Nitinol Filter design are shown for 5 stages of filter delivery. In many films the end view did not have proper lighting and so it did not record on the film. This problem has been worked out in the most recent films.
Figure 8a. Delivery and clot capture studies of a 2-wire Nitinol Filter
Figure 9, More Nitinol Filters

Two Nitinol Filter prototypes are shown just after completion of delivery. The upper photographs show a filter with tangled limbs. The middle shows a pressure meter in the camera's field of view.
Figure 10. Clots challenging a Nitinol Filter

clot diameter 5mm
clot length 5mm
flow rate 2.5 liters/minute
cava diameter 28 mm
type of filter 7 wire daisy cone
desired orientation for most effective filtering

direction of blood flow

side view  end view

STABLE orientation

side view  end view

Figure 11. Stability of Mobin-Uddin Umbrella
Umbrella migrations to the right heart and pulmonary arteries reported in the literature. Many of these migrations proved to be fatal (9,10,12,19).

When the fluid flow was first turned on the pressure surged momentarily and then dropped as the cellulose cava ripped clean in half. The device was examined closely to find that the teeth were designed with the wide dimension oriented perpendicular to the axis of the cava. In this way the teeth made six linear perforations forming a ring around the cava and comprising more than 10% of the caval circumference. The cellulose tubing was replaced, the flow rate turned down, and the filter captured all ten clots that challenged it.

Greenfield Filter As with the Mobin-Uddin Umbrella, the Greenfield Filter was too large to fit through the delivery port and had to be positioned by hand. It was also difficult to orient in its ideal filtering configuration as shown in figures 12 & 13. Abdomen films of Beth Israel Hospital patients with Greenfield filters were reviewed to look for evidence of suboptimal filter orientation.

16 B.I. patients had Greenfield filters
7 patients had the appropriate X-rays readily available for review
4 patients had definite evidence of a tilted filter

Unfortunately patient films do not provide as good a view of the filters as does the test apparatus, but even so, these
desired orientation for most effective filtering

direction of blood flow

side view  end view

STABLE orientation

side view  end view

Figure 12. Stability of Greenfield Filter
Figure 13. Greenfield Filter

This filter in a patient is not only tilted but also has two limbs outside the inferior vena cava.
clinical films show at least 4/7 tilted filters. The difficulty of delivering the Greenfield and the likelihood of tilted orientation has been reported previously (9). The Greenfield Filter captured half of the short clots and half of the long clots. As clots were captured they plugged the small spaces between the wire limbs near the apex of the device and diverted flow streamlines to the big spaces at its base so that the filter became less effective as it filled with clot. Greenfield also observed this trend in animal studies of the Greenfield Filter (20,21). Sometimes the leading end of a clot was captured in a small inner space, the trailing end was then diverted to a large outer space, and as the trailing end passed through the large opening it pulled the rest of the clot through as well.
VIII. Discussion

This system has been effective in pinpointing Nitinol Filter design problems and permitting accurate evaluations of corrective modifications. At this writing the Nitinol Filter is being modified to facilitate deliveries to small cavae. Slow motion analysis provides a detailed account of the filter's shape recovery from a set of straight wires to its interlocking petal configuration. The test apparatus has also provided data on the clot capturing efficiency of several filters and has shown that these filters have the same stability problems which have been reported in the clinical literature. This supports the validity of using this test apparatus for evaluating IVC interruption devices.

The studies showing 5mm diameter clots passing through the Greenfield Filter do not agree with Greenfield's prediction of filter performance based on a similar clot capture study he conducted in animals (20). There are two major differences between these studies. First Greenfield's studies were done in dogs which have smaller venae cavae than humans. In small cavae the filter tends to close up and is more effective in capturing small clots. Secondly, his report showed only one projection of the filter. This is probably not enough to infer performance of the device in three dimensional space. Greenfield did not report examining the lungs for clot which would be the best place to find clot if it had passed through the filter. These two studies together
suggest that the Greenfield Filter is effective at capturing clots in small cavae but less effective in large cavae.

Blood clots used in these experiments are not necessarily an appropriate substitute for actual pulmonary emboli. Dog blood allowed to clot in plastic tubing is more slippery and more elastic than old clot which has built up in the legs over some time. It is probably more appropriate to obtain actual pulmonary emboli from autopsies of human patients or to find a similar artificial material (perhaps silicone rubber) than to use freshly clotted blood. Another possibility, albeit expensive, would be to generate old clot in animals by the method of Sabiston or Wessler.

Experimental clot size is another critical issue for blood clot filter evaluation that needs to be resolved. Ideally, a filter captures all clots large enough to be dangerous but does not become unnecessarily occluded by small harmless clots. This is complicated by the observation that different sizes of people with different health conditions can withstand different maximum sizes of clot(22). It is also conceivable that a shower of small emboli can be just as bad as a single large embolus.

Although the system works well, like any new design there are a number of ways to improve it. There is space available in the camera's field of view which should be used to display flow rate and pressure. Unfortunately, neither of the existing flow or pressure meters fit in the space available for them in the camera's field of view. This could be
remedied by measuring pressure and flow electronically and providing a digital or electronic/analog display that fits in front of the camera. Other improvements would include obtaining a lens for magnification of the end view and acquiring a pump that accurately duplicates the pulsatile flow observed in the venous system.
IX. Conclusion

An appropriate test apparatus for evaluating inferior vena cava filters has been built and made operational. Initial experiments have revealed interesting information about two filters in clinical use and it has also been helpful in evaluating a series of Nitinol Filter prototypes. Although some issues concerning modeling pulmonary emboli and documenting flow/pressure data remain to be addressed, the apparatus is ready to conduct a comprehensive set of experiments to evaluate deliveries and clot capturing ability of all existing IVC filters. This study should then be followed by an in vivo series to verify the accuracy of the in vitro experimental results. The data should also be examined in light of the human experience with the Greenfield Filter and Mobin-Uddin Umbrella.

This apparatus may open the way to a better understanding of pulmonary emboli and mechanical means of effectively preventing them from reaching the lungs.
REFERENCES


