EFFICACY OF PERCUTANEOUS VAS OCCLUSION IN COMPARISON TO CONVENTIONAL VASECTOMY

FINAL REPORT

December 1998

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EXECUTIVE SUMMARY

Introduction
At least in theory, percutaneous occlusion of the vas deferens could offer several potential advantages over vasectomy as a male contraceptive because it is less invasive and thus might have a lower rate of complications; it might be quicker and/or easier to perform; some types could be more easily reversible; and it may be more acceptable since it does not involve an open surgical procedure. If demonstrated to be safe and effective, percutaneous vas occlusion could increase the acceptability and use of contraception by men.

Studies on occlusion of the vas deferens for contraception by percutaneous injection of various chemicals into the vas began in the 1970's in China. While this was demonstrated to be easily performed and to lead to high rates of azoospermia and low pregnancy rates, reversal was no easier than for vasectomy. This led to additional work with formed-in-place plugs (material that is injected into the vas as a liquid, which then solidifies forming a plug that blocks the vas lumen). In 1995, Soebadi and co-workers in Indonesia investigated the use of Ovabloc (a formed-in-place silicone product developed for use in female sterilization) for percutaneous vas occlusion in Indonesian males (referred to as vasoc when used for vas occlusion). They reported good success, with no significant differences seen in rates of azoospermia at one year between men undergoing vasoc vas occlusion (98.3%; 57/58) and those having a vasectomy (100%; 64/64).

The objectives of our study were to:
1. Determine the appropriate volume of vasoc needed for vas occlusion of Dutch males
2. Adapt if necessary the instruments and equipment for vasoc vas occlusion in Dutch males
3. Determine the efficacy in Dutch males of vasoc formed-in-place silicone plugs as an occlusive male sterilization method compared to conventional vasectomy

Vas deferens measurements in Dutch males
Outer and inner vas diameter measurements were taken (using identical methods to those of Soebadi in Indonesia) of 44 vas specimens removed from 22 Dutch males who underwent a vasectomy. Results were compared with those reported by Soebadi et al. (1995) for vas deferens measurements in Indonesian men. Although the outer diameter of the vas in the Dutch males was slightly larger than in Indonesian males, the inner diameter was similar in both. It was decided that the volume of vasoc used in the Indonesian study should be sufficient to block the vas in Dutch males as well, and was used for this study.

Efficacy of vasoc vas occlusion in Dutch males
Study design:
The efficacy of vasoc vas occlusion was compared to that of conventional vasectomy using data on sperm counts, percentage sperm motility, percentage progressively motile sperm, and concentration of progressively motile sperm per ml for up to one
year following the procedure. As a way of evaluating each method’s safety and acceptability, information on subject’s reports of peri- and post-operative pain, post-operative swelling and post-operative hematoma was gathered from the men by using a patient questionnaire. In addition, swelling, hematoma and potential complications were determined through objective clinical evaluation one week after the procedure.

Methods:
During performance of pre-study vasoc vas occlusion procedures, it was found that the Indonesian instruments were difficult to use in Dutch males primarily due to their relatively small caliber and the thick scrotal skin of the Dutch males. A larger diameter ringed clamp was necessary for grasping the vas and a new fixation clamp was developed and called a "Vasoc clamp" because the oval fixation clamp used in Indonesia was not strong enough to guarantee adequate fixation of the blunt needle during the injection process.

All vasoc vas occlusion and vasectomy procedures were conducted in the Department of Urology, Academic Hospital Maastricht, Maastricht, The Netherlands. Both techniques were performed under local anesthesia.

The vasoc vas occlusion procedure involved grasping and stretching the skin over the vas with a ringed clamp. The skin and wall of the underlaying vas deferens were punctured with a hypodermic needle, which was then removed and a blunt metal needle advanced into the vas. After determining that the needle was correctly positioned in the vas, it was clamped and fixed in place with a Vasoc clamp. The procedure was repeated on the opposite vas. The vasoc material was then prepared by mixing the silicone and hardener together. Some material was placed on a glass test plate, to monitor the curing process. The syringe containing the silicone was placed in the handpump applicator which was then connected to the blunt needle in the vas. Silicone was injected into the vas deferens until the appropriate degree of resistance was felt. After the silicone was injected into the vas, the handpump applicator was removed, and the needle taken out of the vas. The same procedure was performed on the opposite side. After the silicone on the testplate had hardened, both vasoc clamps were released.

Conventional vasectomies were performed by isolation of the vas through an incision made in the scrotal skin. A piece of vas 2 to 3 cms in length was removed, and the ends of the vas were occluded with a 2.0 vicryl transfixation ligature. Fascial interposition was used on the proximal end of the vas. When skin incisions were large, 2.0 Vicryl Rapide® was used for closing the skin.

Subjects were instructed to return at one week after the procedure to have a clinical exam to check for complications related to the procedure and so that the investigator could note the presence of any swelling or hematoma. They were asked to complete a patient questionnaire at the one week follow-up visit which included information on subjective assessment of pain during and after the procedure, as well as the presence of swelling or hematoma after the procedure. Subjects were asked to return for semen
analysis at 6 and 12 weeks after the procedure. If azoospermia was not achieved by the 12 week post-procedure visit they were instructed to return for additional semen analyses. In addition, all study subjects were asked to bring in a semen sample for analysis one year after the procedure. Semen samples were evaluated in the infertility laboratory of the Academic Hospital Maastricht and percent sperm motility, percent progressive sperm motility, sperm concentration per ml of ejaculate and concentration of progressively motile sperm per ml determined.

Results:
The vasoc vas occlusion procedure was attempted on a total of 58 subjects and successfully completed on both vasa in 49 men (85%). However, in some cases (13 subjects, 26%), percutaneous injection of vasoc was not possible on one or both sides, and it was necessary to expose the vas in order to inject the vasoc. In the 9 cases where it was not possible to do vasoc vas occlusion on one or both sides reasons included uncertainty if the needle was in the vas, silicone leakage, problems inserting the needle in the vas, and dislocation of the needle during the procedure. For those vasa where vasoc injection was not possible, a conventional vasectomy was performed.

The procedure time for vasectomy was significantly less than for vasoc vas occlusion (mean 28.1 min versus 36.8 min), the latter requiring time for the vasoc to cure. The mean curing time was approximately 14 minutes, with a range from 9 to nearly 23 minutes.

There was no difference in the degree of peri-operative pain reported by subjects having vasoc vas occlusion versus vasectomy. However, men undergoing vasoc vas occlusion reported significantly less post-operative pain (P=0.02) than men having a vasectomy. Additionally, men having a vasectomy reported significantly more post-operative swelling (P=0.01) and post-operative hematoma (P=0.04) than men having vasoc vas occlusion. There were however, no differences noted in post-operative swelling or hematoma observed on clinical exam one week following the procedure. Similar results were obtained when the data were analyzed to account for the fact that it was necessary to expose the vas in some men who had vasoc vas occlusion.

Significantly (P<0.0001) more men achieved azoospermia following vasectomy than following vasoc vas occlusion (89.8% versus 10.8% at 52 weeks, respectively). In addition, the percentage of men with 0% sperm motility in the vasectomy group was greater than 94% at every follow-up interval compared to less than 20% for men in the vasoc vas occlusion group. Following vasectomy, men had low numbers of sperm per ml, low values for % sperm motility and % progressive sperm motility and low numbers of progressively motile sperm per ml --- all indications that the vasectomy procedure was successful. In contrast, those men undergoing vasoc vas occlusion had higher values for all of these variables, indicating that the procedure was not successful.

Many of the men who did not achieve azoospermia following vasoc vas occlusion opted to have a vasectomy before 52 weeks after the procedure (22/49; 44.9% of all
men undergoing the vasoc procedure). Of the 48 vasectomy successes, 44 men achieved azoospermia and 4 men with persistent low levels of non-motile sperm (<50,000 sperm/ml) were told they could stop using alternate contraception. One man had a vasectomy failure (defined as inability to rely on the vasectomy for contraception) and elected to have another vasectomy, which was done 6 months after the first.

Partners of three study subjects originally enrolled in the vasoc vas occlusion group became pregnant (3/58; 5.2%); two men who had vasoc vas occlusion on both sides and one who had vasoc vas occlusion on one side and a vasectomy on the other. Both of the subjects who had bilateral vasoc vas occlusion stopped coming for follow-up, even though they had not been cleared. One reported a pregnancy 8 months and the other 11 months post-procedure. The man who had vasoc vas occlusion on one side and a vasectomy on the other was declared azoospermic one year post-procedure. His partner became pregnant 9 months later and semen analysis at that time showed 72 x 10⁶ sperm/ml and 65% motility.

Discussion:
Based on all the variables examined, it is clear that men undergoing vasoc vas occlusion in this study would not be able to rely on that method for contraception; only 11% of men had achieved azoospermia by one year after the procedure. These results are in marked contrast to those reported by Soebadi and co-workers in Indonesian males, where no significant differences were reported between percentages of men achieving azoospermia in the vasoc vas occlusion and vasectomy groups. Reasons for the difference in these study results are unclear, but may be related to one or more of the following: small differences in the diameter of the vas between Indonesian and Dutch males; changes necessary in the instruments to accommodate anatomical differences in Indonesian and Dutch males; and difference in the distribution of the components of the hardener and the silicone used in the two studies.

While the procedure time for vasectomy was significantly less than for vasoc vas occlusion, there appeared to be some advantages of the vasoc vas occlusion technique in terms of less pain, post-operative swelling and post-operative hematoma compared to vasectomy.

An additional potential advantage of vasoc vas occlusion is that, in theory, reversal should be easier than surgical vasectomy reversal. There have been no published reports of return to fertility following removal of vasoc plugs in humans. Observations made during our study suggest that vasoc leads to fibrosis and tissue reaction which could make simple plug removal difficult, requiring excision and reanastomosis of the vas. Therefore, there would be no advantage of vasoc vas occlusion over conventional vasectomy in terms of reversal.

There are a number of concerns and service delivery issues regarding vasoc vas occlusion that need to be kept in mind, even if efficacy could be improved to an acceptable level. Vasoc vas occlusion is complex and technically demanding, requiring
specialized and costly equipment and supplies, refrigeration or freezing for the materials, and three people to do the procedure. In many low resource settings these factors would impact on the ability of service sites to offer vasoc vas occlusion, unless significant changes were made in the procedure.

**Conclusion**

Based on the results of this study, vasoc vas occlusion is not suitable for use as a male contraceptive at this time. Not only was efficacy found to be unacceptably low, but service delivery constraints of the method in its current state would likely limit utility in low resource settings. A safe and efficacious percutaneous occlusion method could, however, offer advantages over vasectomy and increase the acceptability and use of contraception by men.

**INTRODUCTION**

In most of the world, modern contraceptive options for men are currently limited to condoms and vasectomy. Studies on occlusion of the vas deferens for contraception by percutaneous injection of various chemicals into the vas began in the 1970’s in China (Zhao, 1990). Chemicals studied have included sclerosing agents that cause tissue damage leading to blockage of the vas lumen (Xiao, 1987; Zhao, 1990), and materials that are injected into the vas as a liquid, which then solidify forming a plug that blocks the vas lumen (Zhao, 1990; Zhao et al., 1992; Soebadi et al., 1995). The latter are commonly referred to as formed-in-place plugs.

In theory, percutaneous occlusion of the vas deferens could offer several potential advantages over vasectomy as a male contraceptive because it is a less invasive procedure which, therefore, might have a lower rate of complications and could be quicker and/or easier to perform than vasectomy. In addition, percutaneous vas occlusion may be more acceptable since it does not involve an open surgical procedure or in some settings where religious issues are of concern, because it doesn’t involve cutting of healthy tissue. Percutaneous vas occlusion with a plug could be more easily reversible compared to vasectomy, which should be considered a permanent contraceptive method, even though vasectomy reversal is possible. If demonstrated to be safe and effective, percutaneous vas occlusion could increase the acceptability and use of contraception by men.

Early efforts to develop percutaneous injection of the vas for male contraception involved injection of sclerosing agents into the vas (carbolic acid and N-butyl alpha cyanocrylate) (Xiao, 1987). It was demonstrated that this easy procedure (since the chemicals are administered via injection) led to high rates of azoospermia, with low pregnancy rates (Xiao, 1987). However, injection of sclerosing agents was not easier to reverse than conventional vasectomy because the occluded portion of the vas needed to be excised and reanastomosis of the vas performed (Zhao et al., 1992).

In 1990 Zhao reported results of studies on percutaneous injection of a formed-in-place polyurethane elastomer plug (known as MPU). He reported that the method was [1] highly efficacious: 98% (490/500) of men became azoospermic; [2] had a very low
rate of complications (infection & hematoma): 0.5% (56/12,000); and [3] was reversible using a simple surgical removal procedure, leading to high pregnancy rates: 100% (31/31) within two years of plug removal.

Additional studies by the investigator confirmed successful reversal of MPU vas occlusion, as defined by pregnancy, in 100% (130/130) of men up to five years after occlusion. The majority (85%, 111/130) of men’s partners became pregnant within 2 years of plug removal. Authors reported removal was easy using a simple surgical procedure, in part because MPU plugs did not adhere to the inner surface of the vas (Zhao et al., 1992).

MPU was approved for use by the China Pharmaceutical and Biological Product Control Institute in November 1992. Although no adverse effects were reported in nearly 300,000 men who had MPU vas occlusion, uncertainties regarding safety of its use due primarily to the presence of an aromatic amine in MPU, led to exploration of identical injection procedures using medical grade silicone (Zhao et al., 1992).

In a small study of 14 men Zhao and colleagues reported no complications and azoospermia in all subjects between 5 and 9 months after percutaneous vas occlusion with formed-in-place silicone plugs (Zhao et al., 1992).

Studies were conducted in baboons to determine efficacy and reversibility of formed-in-place silicone rubber plugs using a product known as Ovabloc', that had been approved for human use by the World Health Organization Toxicology Panel. Azoospermia was achieved in 70% (14/20) of the baboons following bilateral injection of silicone into the vas (13 after 1 month and 1 after 7 months). The remaining 6 (30%) did not achieve azoospermia by approximately 1 year after occlusion. After surgical removal of the plugs in the 14 baboons who achieved azoospermia, sperm reappeared in the semen of 11 (78.6%). The other 3 (21.4%) animals remained azoospermic following removal of the plugs.

Soebadi et al. (1995) investigated the use of the Ovabloc silicone rubber product (referred to as vasoc when used for vas occlusion), for percutaneous vas occlusion in Indonesian males. Using 130 vasa from 65 Indonesian men undergoing conventional vasectomy it was demonstrated that the outer diameter of the vas deferens ranged from 1.16 to 2.20 mm (mean 1.80 ± 0.15 mm) and the inner diameter ranged from 0.60 to 1.20 mm (mean 0.93 ± 0.11 mm). The volume of silicone needed to effectively occlude the vas while limiting the likelihood of vas rupture was determined to be 0.1531 ± 0.0059 ml, delivered by 5 to 6 turns of the applicator handwheel (see Methods section below for details of the vasoc injection process).

Based on the results of this volume study Soebadi and his colleagues performed an efficacy study comparing 58 men who underwent vasoc vas occlusion with 64 men

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1 Ovabloc, developed by A.M.G.S. B.V. in the Netherlands, is a formed-in-place silicone plug for female sterilization. The silicone is injected as a liquid into the oviduct via a hysteroscope and then hardens once inside the oviduct forming a blockage to the passage of both sperm and oocytes.
who received a no-scalpel vasectomy (NSV). Men undergoing vasoo occlusion reported significantly less pain during the procedure and had significantly fewer complaints in the first month post-procedure compared to the vasectomy group. There were no differences in complication rates between the two groups. No significant differences were seen in rates of azoospermia between the two groups. By six months 98.3% (57/58) and 100% (64/64) of men were azoospermic in the vasoo occlusion and NSV groups, respectively (Soebadi, 1996; Soebadi et al., 1995). In an additional 84 men who underwent vasoo occlusion in three locations in East Java the 3 and 6 month azoospermia rates were 85.7% (72/84) and 88.1% (74/84), respectively (Soebadi, 1996).

The objectives of the Dutch study were to:
1. Determine the appropriate volume of vasoo needed for vas occlusion of Dutch males
2. Adapt, if necessary, the instruments and equipment for vasoo occlusion in Dutch males
3. Determine the efficacy in Dutch males of vasoo formed-in-place silicone plugs as an occlusive male sterilization method compared to conventional vasectomy

In December 1994 Dr. Zambon from the Department of Urology, Academic Hospital Maastricht, The Netherlands and Dr. Slot, from The SCMG Outpatient Clinic for Family Planning, Leiden, The Netherlands were trained in percutaneous vas occlusion using vasoo by Dr. Soebadi in Indonesia.

**VAS DEFERENS MEASUREMENT IN DUTCH MALES**

A study of vas deferens measurements in Dutch males was conducted and results compared with those reported by Soebadi et al. for vas deferens measurements in Indonesian men (Soebadi et al., 1995). It was hypothesized that if no differences were found between the size of the vas in these two populations of men, the same plug size that was used by Soebadi in Indonesian males could be used for the efficacy study in Dutch males. Presumably, the inner diameter of the vasa is the critical factor for determining the proper plug size for a specific group of males.

**Methods**

In a group of 22 Dutch males who underwent a conventional vasectomy, 44 vas specimens were measured within 10 minutes after they had been excised. The outer diameter was measured with a Mitotuyo Digimatic micrometer and the inner diameter was measured with a set of pin gauges. Identical methods were used for measuring the vas as were used by Soebadi in Indonesia.

**Results**

In the Dutch males the outer diameter ranged from 1.5 mm to 2.5 mm with a mean value of 2.00 ± 0.25 mm. The inner diameter of the vas deferens ranged from 0.7 to 1.2 mm with a mean of 0.94 ± 0.10 mm.
Discussion
Comparing the results in Dutch and Indonesian males a similar inner vas diameter was found in both groups (Table 1, Figure 1). The outer diameter of the vas in the Dutch males was slightly larger than the vas in Indonesian males, due to a thicker layer of connective tissue in the first group (Table 1).

<table>
<thead>
<tr>
<th>Outer diameter (mm)</th>
<th>Indonesian Males</th>
<th>Dutch Males</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=130</td>
<td>n=44</td>
</tr>
<tr>
<td>1.80 ± 0.15</td>
<td>(1.16 - 2.20)</td>
<td>2.00 ± 0.25</td>
</tr>
<tr>
<td>(0.60 - 1.20)</td>
<td>(1.50 - 2.50)</td>
<td></td>
</tr>
<tr>
<td>Inner diameter (mm)</td>
<td>0.93 ± 0.11</td>
<td>0.94 ± 0.10</td>
</tr>
<tr>
<td>(0.60 - 1.20)</td>
<td>(0.70 - 1.20)</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Vas Deferens Measurements in Indonesian and Dutch Males. Mean ± S.E.M. (range)

Because the inner diameter of the vas in Dutch males was similar to that of the Indonesian men, it was decided that the volume of vasoc used in the Indonesian study should be sufficient to block the vas in Dutch males and was used for this study. This volume was 0.1531 ± 0.0059 ml, equivalent to 160 mg, which was delivered by 5 to 6 turns of the applicator handwheel (see Methods section below for details of the vasoc injection process).

**VASOC VAS OCCLUSION EFFICACY STUDY IN DUTCH MALES**

**Study Design:**
The study was originally designed to include 75 males in the vasoc vas occlusion group and another 75 males in the conventional vasectomy group. The efficacy of the two techniques was compared using data on sperm counts (to determine rates of azoospermia), percentage sperm motility, percentage progressively motile sperm, and concentration of progressively motile sperm per ml for up to one year following the
procedure. As a way of evaluating each method's safety and acceptability, information on subjects' reports of peri- and post-operative pain, post-operative swelling and post-operative hematoma was gathered from the men by using a patient questionnaire. In addition, swelling, hematoma and potential complications were determined through objective clinical evaluation by the investigator one week after the procedure.

From the beginning of 1996, men coming to the outpatient clinic of the Academic Hospital Maastricht for vasectomy were asked if they would be interested in participating in the study. They were offered the choice to undergo a conventional vasectomy or percutaneous vasoc vas occlusion. Men who chose vasoc vas occlusion were enrolled in the vasoc vas occlusion group. Those men who preferred a conventional vasectomy were asked if they would be willing to allow the investigator to use the information normally gathered during and after a vasectomy in the analysis comparing the outcome of conventional vasectomy and vasoc vas occlusion, and if they would fill out the patient questionnaire described above. If the men agreed, they were enrolled in the vasectomy comparison group.

The study protocol was approved by the Medical Ethical Committee and the Board of the Academic Hospital Maastricht in October 1995.

**Methods**

**(Modifications of instruments & supplies needed for vasoc vas occlusion:**

Table 2 lists some of the instruments and supplies needed for vasoc vas occlusion.

<table>
<thead>
<tr>
<th>Item</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ringed clamp (grasping forceps)</td>
<td>Isolation and stabilization of the vas during puncture</td>
</tr>
<tr>
<td>Hypodermic needle</td>
<td>Puncture of the skin and vas</td>
</tr>
<tr>
<td>Blunt needle</td>
<td>Inserted into the vas through the puncture site; silicone is injected into the vas via this needle</td>
</tr>
<tr>
<td>Vas fixation clamp</td>
<td>Fixation of the blunt needle in the vas; occlusion of the vas during silicone injection; the space within the end of the clamp holds the silicone in place while it cures to form a plug</td>
</tr>
<tr>
<td>Vasoc catheter</td>
<td>Connects the handpump applicator to the blunt needle</td>
</tr>
<tr>
<td>Vasoc handpump applicator</td>
<td>Contains the silicone-filled syringe; turning the handwheel of the applicator leads to injection of the silicone.</td>
</tr>
<tr>
<td>Dissecting forceps</td>
<td>Used to expose the vas if percutaneous injection was not possible.</td>
</tr>
</tbody>
</table>

**Table 2: Items Needed for Vasoc Vas Occlusion**

In the first half of 1995, several vasoc vas occlusion procedures were performed in the SCMG Clinic in Leiden, The Netherlands (a clinic for surgical and non-surgical contraception) by Dr. Zambon. In addition, Dr. Zambon performed six vasoc vas occlusion procedures in Frauenfeld, Switzerland. During these procedures it was found that the Indonesian instruments were difficult to use in Dutch and Swiss males primarily due to the relatively small caliber of the Indonesian instruments and thick scrotal skin of the Dutch and Swiss males.
Dutch and especially Swiss males have a thicker scrotal skin than Indonesian males, so that the Indonesian ringed clamp could not enclose the scrotal skin and vas deferens in the Dutch and Swiss men. Thus, a larger diameter ringed clamp was necessary for grasping the vas; 5 mm compared to the 4 mm clamps used in Indonesia. Moreover, the oval fixation clamp used in Indonesia (Figure 2, top) was not strong enough to guarantee adequate fixation of the blunt needle during the injection process. For that reason a new fixation clamp was developed based on the Duval clamp, a clamp used in pulmonary surgery. This modified Duval clamp, called a "Vasoc clamp" (Figure 2, bottom), had an inner width of 15 mm (the same dimension as the oval fixation clamp), gave firm fixation of the blunt needle and was easy to use. The dissecting forceps as used by Soebadi did not need any modification.

![Figure 2. Oval fixation clamp used in Indonesia (top) and the new fixation clamp (bottom) - called a "Vasoc clamp" -- based on the Duval clamp, developed for use in the Netherlands.](image)

**Vasoc vas occlusion procedure techniques:**
All vasoc vas occlusion procedures were performed in an operating theatre in the day-clinic (same day surgery) of the Academic Hospital Maastricht. The room temperature had been raised to about 24 degrees and subjects were lying supine. The scrotum was shaved and the penis retracted upwards and secured to the abdomen by an adhesive band. The scrotal skin was prepared with a Betadine® solution which was at room temperature to prevent contraction of the scrotal skin and cremaster muscle. The operating field was draped with a disposable sterile drape and the surgeon and operating nurses wore a sterile gown, cap, mask and gloves. The procedures were performed with the surgeon standing on the right side of the subject.

The vasoc percutaneous vas occlusion technique is illustrated in the following figures.
Figure 3. The vas was grasped and isolated with the three finger technique for administration of local anesthesia (2% lidocaine with epinephrine). A small depot of about 0.5 ml lidocaine was injected at the puncture site in the skin overlying the vas, which is the place where the vas was to be isolated. The needle was advanced parallel to the vas in the direction of the inguinal canal and 2-5 mls of lidocaine were injected.

Figure 4. The vas was grasped with the 5 mm ringed clamp through the scrotal skin in such a way that there was a minimal amount of tissue between the skin surface and the vas deferens. The skin was stretched over the vas as firmly as possible.
Figure 5. The skin and wall of the underlying vas deferens were punctured at 45 degrees in the direction of the inguinal canal with a 21 gauge hypodermic needle.

Figure 6. The hypodermic needle was removed and a 23 gauge blunt metal needle was advanced into the vas.
Figure 7. The position of the blunt needle in the vas was tested by injecting 10 ml of normal saline into the vas. If the needle was correctly positioned in the vas the subject would experience a clear sensation of urgency to urinate.

Figure 8. When the needle was in the correct position, it was clamped and fixed in place with the Vasoc clamp. Care was taken to place the clamp in a way that the point of the needle was enclosed in the opening of the clamp but that there was enough length of the vas between the point of the needle and the opposite side of the clamp that could be filled with silicone.
Figure 9. After placement of the Vasoc clamp adequate fixation was tested by injecting air through the needle using a 10 ml syringe. Resistance was met on pushing the plunger of the syringe if adequate fixation was achieved.

Figure 10. The above procedures for isolation and fixation of the blunt needle in the vas were performed on the opposite vas.
Figure 11. After successful puncturing of the vas and fixation of the blunt needles on both sides, the vasoc material was prepared by injecting the hardener into the medical grade silicone. The syringe containing the silicone was kept in the freezer until approximately 10 minutes before use, thereby reducing the rate of spontaneous hardening which occurs over time.

Figure 12. After injecting the hardener into the silicone syringe, mixing was done by moving the plunger of the syringe up and down 20 times.
Figure 13. After mixing, some material was placed on a glass test plate, to monitor the curing process.

Figure 14. The syringe containing the silicone was placed in the handpump applicator.
Residual fluid was withdrawn from the blunt needle and the inner surface of the needle dried with a gauze. The handpump applicator was connected to the catheter, and after filling the catheter completely with silicone (approximately 3 turns of the handwheel) the catheter was connected to the blunt needle. Silicone was injected into the vas deferens by turning the handwheel of the applicator six or seven times. In most cases resistance was felt clearly after six turns of the handwheel. In some cases additional turns of the handwheel were needed before the appropriate degree of resistance was felt. After the silicone was injected into the vas the needle was taken out. The same procedure was performed on the opposite side. After the silicone on the testplate had hardened, both vasoc clamps were released.

In cases where it was difficult to puncture or enter the vas, or where there was uncertainty about adequate positioning of the blunt needle, the vas was exposed so that the procedure could be completed. Using the dissecting forceps, the skin overlying the vas was punctured and spread in order to bring the vas into direct view. Under direct vision, the vas was punctured with a 21 gauge hypodermic needle, which was then removed and a blunt 23 gauge needle advanced into the vas. The vas was not pulled above the skin level to be punctured. Testing for correct positioning of the needle in the vas and the rest of the procedure were performed exactly as described above.

**Conventional vasectomy techniques:**

Vasectomies were also performed in an operating theatre in the day-clinic of the Academic Hospital Maastricht. Subjects were prepared and local anesthesia was administered as described above. After adequate local anesthesia, a 1 to 1.5 cm incision in the skin over the vas was made with a scalpel. The vas was grasped with forceps and fixed with a drape clamp. The sheath surrounding the vas was incised. The vas was isolated, clamped, and a piece of vas 2 to 3 cms in length was removed. Both stumps of the vas were occluded with a 2.0 vicryl transfixation ligature. Fascial interposition was used by closing the spermatic fascia over the proximal end of the vas.
with a second ligature. Small skin incisions required no skin closure. When skin incisions were large, 2.0 Vicryl Rapide® was used for closing the skin.

**Follow-up protocol:**
All study subjects were instructed to come to the Urology Department one week after the procedure to have a clinical exam to check for complications related to the procedure, and so that the investigator could note the presence of any swelling or hematoma. Subjects were asked to complete a questionnaire which included information on subjective assessment of pain during and after the procedure on both a standard scale (none, mild, moderate, or severe) and a visual analogue scale (1=no pain, 10=severe). In addition, subjects were asked to classify swelling and hematoma in the period after the procedure as none, mild, moderate or severe.

Subjects were asked to return for semen analysis at 6 and 12 weeks after the procedure. If azoospermia was not achieved by the 12 week post-procedure visit they were instructed to return for additional semen analyses. In addition, all study subjects were asked to bring in a semen sample for analysis one year after the procedure.

Semen samples were collected at home by study subjects, delivered to the Academic Hospital Maastricht within several hours of collection and analyzed in the infertility laboratory. Percent sperm motility and percent progressive sperm motility were determined based on subjective assessment of twenty fields of non-centrifuged semen examined microscopically under 200x magnification. Sperm concentration per ml of ejaculate was determined using a hemocytomer. The concentration of progressively motile sperm per ml was calculated by multiplying the percent progressive sperm motility by the concentration of sperm per ml of ejaculate.

**Vasectomy for failed vasoc vas occlusion procedures:**
Those subjects who failed to become azoospermic after vasoc vas occlusion were offered a conventional vasectomy. The vasectomy procedure described above was used when these men indicated they wanted a vasectomy.

**Statistical analysis:**
In order to determine if procedure time for vasoc vas occlusion was significantly different from that of conventional vasectomy, means were compared using a t-test. To determine if differences in peri-operative pain, post-operative pain, swelling, and hematoma reported by subjects, as well the physicians’ assessment of post-operative swelling and hematoma were significantly different for those men undergoing vasoc vas occlusion versus vasectomy, data were compared using chi-square analysis or Fisher’s exact test, depending on the expected frequencies. Chi-square analysis was also used to examine the differences in numbers of men achieving azoospermia and 0% motile sperm in the two groups of men.
Results

Ability to do the vasoc vas occlusion procedure

The vasoc vas occlusion procedure was attempted on a total of 58 subjects. The outcome of these attempts is shown in figure 16.

![Pie chart showing the outcome of attempted vasoc vas occlusion procedures. 85% successful on both sides, 12% successful on one side, and 3% unable to do vasoc on either side.]

Figure 16. Outcome of Attempted Vasoc Vas Occlusion Procedures (N=58)

In the 9 cases where it was not possible to do the vasoc vas occlusion on one or both sides, reasons included uncertainty if the needle was in the vas (3 cases), silicone leakage (3 cases), problems inserting the needle in the vas (2 cases), and dislocation of the needle during the procedure (1 case). For those vasa where vasoc injection was not possible, a conventional vasectomy was performed.

In some cases where vasoc vas occlusion was done, percutaneous injection was not possible on one or both sides, and it was necessary to expose the vas in order to do the injection of vasoc (see Figure 17).
**Turns of the handwheel and curing time during the vasoc vas occlusion procedures**

The mean number of turns of the applicator handwheel used during the vasoc vas occlusion procedures was $9.28 \pm 0.12$ (n=105 vasa). The minimum and maximum number of turns was 6 and 18', respectively. For the majority of vasa (88/105, 83.8%) 9 or 10 turns of the handwheel were used.

The mean $\pm$ SEM time necessary for the vasoc to cure was $13.46 \pm 0.35$ minutes (49 men), with a minimum of 9 minutes and a maximum of 22.45 minutes. In the majority of cases (40/49, 81.6%) between 11 and 16 minutes were necessary for the vasoc to cure.

**Procedure time$^2$**

The mean $\pm$ SEM procedure time for men having a vasectomy (49 men, operating room log data missing for 1 man) was significantly less ($P=0.00$) than for men undergoing vasoc vas occlusion (n= 47 men, operating room log data missing for 2 men); $28.14 \pm 1.00$ min versus $36.81 \pm 1.28$, respectively. For men having a vasectomy, the range was 20-40 minutes, and most vasectomy procedures (39/49; 79.6%) were between 20-30 min. The range for vasoc vas occlusion was 20-60 min, with a procedure time for most men (38/47; 81%) between 30-45 min.

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$^2$ Little resistance was felt during the injection in the subject where 18 turns was used. There were two series of 9 turns. Histology performed after vasectomy at 9 months post-vas occlusion showed silicone outside the vas.

$^3$ The time used here for the procedure is actually the time taken from the operating room logs. This represents the entire time the subject was in the operating room and not the actual time it took to complete the vasoc or vasectomy procedure. Factors unrelated to the vasoc or vasectomy procedure could have affected the total operating room time. However, overall this time is likely to be reflective of how long the vasoc or vasectomy procedure took.
**Peri-operative pain: subject reports**

There was no difference in the degree of peri-operative pain reported by subjects having vasoc vas occlusion versus vasectomy with either the standard (Figure 18) or the visual analog scale (Figure 19). The mean value for pain during the procedure reported with the visual analog scale for men undergoing vasoc vas occlusion was $4.38 \pm 0.43$ and for men having a vasectomy was $3.13 \pm 0.48$.

![Figure 18. Subject Reports with Standard Scale of Peri-Operative Pain For Men Having Vasectomy (N=24) or Vasoc Vas Occlusion (N=44)](image)

**Post-operative pain: subject reports**

Men undergoing vasoc vas occlusion reported significantly less post-operative pain ($P=0.02$) than men having a vasectomy using the standard (Figure 20) and visual analog scales (Figure 21). The mean value for post-operative pain reported with the visual analog scale for men undergoing vasoc vas occlusion was $1.66 \pm 0.24$ and for men having a vasectomy was $3.29 \pm 0.44$.  

![Figure 19. Subject Reports with Visual Analog Scale of Peri-Operative Pain For Men Having Vasectomy (N=24) or Vasoc Vas Occlusion (N=42) (0 = No Pain, 10 = Heavy Pain)](image)
Figure 20. Subject Reports with Standard Scale of Post-Operative Pain For Men Having Vasectomy (N=24) or Vasoc Vas Occlusion (N=45)

Figure 21. Subject Reports with Visual Analog Scale of Post-Operative Pain For Men Having Vasectomy (n=24) or Vasoc Vas Occlusion (n=45) (0 = No Pain, 10 = Heavy Pain)

*Post-operative swelling and hematoma: subject reports and clinical findings*

Men having a vasectomy reported significantly more post-operative swelling ($P=0.01$) than men having vasoc vas occlusion (Figure 22).

Figure 22. Subject Reports of Post-Operative Swelling For Men Having Vasectomy (N=24) or Vasoc Vas Occlusion (N=44)
However, there were no differences noted in post-op swelling observed on clinical exam (Figure 23).

![Swelling Graph](image)

*Figure 23. Post-Operative Swelling Observed During Clinical Exam For Men Having Vasectomy (N=24) or Vasoc Vas Occlusion (N=45)*

Men having a vasectomy reported significantly more post-operative hematoma (P=0.04) than men having a vasoc vas occlusion (Figure 24).

![Hematoma Graph](image)

*Figure 24. Subject Reports of Post-Operative Hematoma For Men Having Vasectomy (N=24) or Vasoc Vas Occlusion (N=44)*

However, there were no differences in post-operative hematoma observed on clinical exam (Figure 25).
Similar results were obtained when the data on pain, post-operative swelling and post-operative hematoma were analyzed to account for the fact that it was necessary to expose the vas in some men who had vasoc vas occlusion.

**Subject status at the end of the study**
The final outcome at 52 weeks post-procedure of men who had vasoc vas occlusion or a vasectomy is shown in Figure 26.

Many of the men who did not achieve azoospermia following vasoc vas occlusion opted to have a vasectomy before 52 weeks after the procedure (total 22/49; 44.9% of all men undergoing the vasoc procedure). In most of these cases the silicone plugs were left in place during the vasectomy because fibrosis and tissue reaction around the site of the plug would have made it difficult to excise that part of the vas deferens under local anesthesia. Doing so would have been much more inconvenient to the
subjects in terms of pain, bleeding or hematoma compared to excision of another part of the vas.

Of the 48 vasectomy successes, 44 men achieved azoospermia and 4 men with persistent low levels of non-motile sperm (<50,000 sperm/ml) were given special clearance. One man had a vasectomy failure (defined as inability to rely on the vasectomy for contraception) and elected to have another vasectomy, which was done 6 months after the first.

Partners of three study subjects originally enrolled in the vasoc vas occlusion group became pregnant (3/58; 5.2%); two men who had vasoc vas occlusion on both sides and one who had vasoc vas occlusion on one side and a vasectomy on the other. The last follow-up visit for one of the subjects who had bilateral vasoc vas occlusion was at 4 weeks post-procedure where his sperm count was 7 x 10^6 sperm/ml with 65% motility. He did not return for further semen analysis and reported his partner was pregnant at 8 months after the procedure. The other subject with bilateral vasoc vas occlusion had semen analyses through 8 months post-procedure and still had low levels (<1 x 10^6 sperm/ml) of motile sperm/ml at that time. He did not come for additional follow-up and at 11 months post-procedure his partner became pregnant. The man who had vasoc vas occlusion on one side and a vasectomy on the other was declared azoospermic one year post-procedure. His partner became pregnant 9 months later and semen analysis at that time showed 72 x 10^6 sperm/ml and 65% motility. It is possible that this subject had a recanalization on the side where vasectomy had been performed or that the silicone plug migrated on the side where vasoc vas occlusion had been performed.

**Semen characteristics of men following vasoc vas occlusion or vasectomy.**
Figures 27-29 show semen characteristics of men following vasoc vas occlusion or vasectomy for 10 week follow-up intervals (the first interval is 5-10 weeks because no man came for follow-up which included semen analysis before 5 weeks after either procedure).

Significantly (P<0.0001) more men achieved azoospermia following vasectomy than following vasoc vas occlusion, overall, and at every 10 week follow-up interval (Figure 27).
In addition, the percentage of men with 0% sperm motility in the vasectomy group was greater than 94% at every follow-up interval, indicating that the remaining sperm in these men’s ejaculates was unlikely to be able to participate in fertilization (Figure 28). In contrast, the vast majority of men (>80%) in the vasoc vas occlusion group had motile sperm at all time points following the procedure (Figure 28). Thus it is likely that the sperm in these men’s ejaculates would be able to participate in fertilization.

Figure 29 shows details of semen characteristics of the two groups of men. As expected, following vasectomy, men had low numbers of sperm per ml, low values for % sperm motility and % progressive sperm motility, and low numbers of progressively motile sperm per ml --- all indications that the vasectomy procedure was successful. In contrast, those men undergoing vasoc vas occlusion had higher values for all of these variables, indicating that the vasoc vas occlusion was not successful.
Figure 29. Semen Characteristics of Men Following Vasectomy or Vasoc Vas Occlusion: A = Mean Sperm Concentration; B = Percent Sperm Motility; C = Percent Progressively Motile Sperm; and D = Concentration of Motile Sperm
Discussion

Based on all the variables examined, it is clear that the men undergoing vasoc vas occlusion in this study could not rely on that method for contraception; only 11% of men achieved azoospermia by one year after the procedure. Of the remaining 89% (those who did not achieve azoospermia), the mean sperm count at last follow-up was $14.9 \times 10^6$ sperm/ml — far from azoospermia — and few men (~6%) were severely oligospermic (defined as $<1 \times 10^6$ sperm/ml). Roughly 45% of the men who had vasoc vas occlusion chose to have a conventional vasectomy at some point during the study since they were unable to stop using alternate contraception following the vasoc procedure.

These results are in marked contrast to those reported by Soebadi and co-workers in Indonesian males (Soebadi et al., 1995). Figure 30 compares results of the vasoc vas occlusion efficacy studies conducted in Indonesia to those conducted in the Netherlands. Soebadi and co-workers found that vasoc vas occlusion was comparable to vasectomy in terms of the percent of men reaching azoospermia. In that study, there were no significant differences in the percent of men reaching azoospermia in the vasoc vas occlusion versus conventional vasectomy groups at all points in time (dashed lines in Figure 30). Results of the studies in the Netherlands, however, showed significantly fewer men reaching azoospermia in the vasoc vas occlusion group compared to the vasectomy group at all follow-up time points and overall at 52 weeks after the procedure; 10.8% versus 89.8%, respectively (solid lines in Figure 30).

![Figure 30. Percent Of Men Reaching Azoospermia Following Vasoc Vas Occlusion Or Vasectomy: Comparison of data from Indonesia and the Netherlands (first follow-up visit 4 weeks in Indonesia, 6 weeks in the Netherlands)](image)

*study authors reported no significant differences
+p<0.0001
Reasons for the difference in these study results are unclear. It is possible that differences in the diameter of the vas between Indonesian and Dutch males could have impacted on the effectiveness of the vasoc vas occlusion method. While the inner vas diameter was nearly identical in the two groups, Dutch males appeared to have slightly larger outer vas diameter. This would suggest that, on average, the wall of the vas is slightly thicker in Dutch males. This may somehow have impacted on formation of the plug or its ability to occlude the vas. We did not perform in vitro occlusion studies to determine the volume of vasoc needed to block the vas, as did Soebadi and co-workers. Rather, we decided that since the inner vas diameter was the same between the Indonesian and Dutch males, that similar volumes of vasoc as used by Soebadi would be sufficient to block the vasa in Dutch males.

A recent report showed that thickness of the vas wall was important in distensibility of the vas, and significantly influenced the rupture volume of the vas (Liu et al., 1997). The authors noted that knowing the maximal distensibility or limiting volume of the vas is critical to determining the volume of material to be injected during vasoc vas occlusion. If slight differences in diameter of the vas or thickness of the wall were shown to have a significant impact on the volume of material needed to occlude the vas, this could present practical problems in trying to expand use of formed-in-place plug occlusion methods to different parts of the world, where vas size may be different.

Additionally, there were some differences in the procedure itself as it was conducted in the two countries which may have played a role in the varying results. Changes necessary in the instruments to accommodate anatomical differences in Indonesian and Dutch males were described earlier. There was also a difference in the vasoc material itself between the two studies; the cross-linking agent that causes the curing of the silicone was in a different component in the two studies. In Indonesia, the cross-linking agent was contained in the hardener and it was necessary to refrigerate this component to prevent spontaneous curing over time. The silicone itself was kept at room temperature. On the other hand, in The Netherlands, the cross-linking agent was contained in the silicone, which was kept frozen, with the hardener being kept at room temperature. Although these differences are minor they could have played a role in the different results observed.

The procedure time for conventional vasectomy was significantly less than for vasoc vas occlusion (mean 28.1 minute versus 36.8 minute). This is not surprising since it is necessary to wait for the vasoc to cure, which increases the overall time needed for the vasoc vas occlusion procedure. The mean curing time was approximately 14 minutes, with a range from 9 to nearly 23 minutes.

There appeared to be some advantages to the vasoc vas occlusion technique in terms of pain, post-operative swelling, and post-operative hematoma, compared to vasectomy. While there were no differences in subjects' reports of pain during the procedure between the two techniques, men undergoing vasoc vas occlusion reported significantly less post-operative pain than did men having a vasectomy. Men
undergoing vasoc vas occlusion also reported significantly less post-operative swelling and hematoma than men having a vasectomy. There were, however, no differences noted on clinical exam seven days post-op in terms of swelling or hematoma at the procedure site between the two groups; the vast majority of the men in both groups had none to slight swelling or hematoma. Much of the swelling and hematoma reported by the vasectomy group was likely to have subsided by the post-op visit.

An effective vas occlusion method that is percutaneous, thus alleviating the need for surgery, may be more acceptable to men. However, in this study, in over one quarter of the vasoc vas occlusion procedures performed, it was not possible to do the injection percutaneously on one or both sides. In these cases, it was necessary to expose the vas in order to do the injection, thus taking away one of the advantages of the technique — that it can be done percutaneously.

An additional potential advantage of vas occlusion with a formed-in-place plug is that reversal, in theory, should be easier than with conventional vasectomy, since all that would be necessary is simply removal of the plugs from the vasa. It is, however, unclear with regards to vasoc vas occlusion what the exact means are by which the plug causes blockage of sperm passage. It could be related to actual occlusion of the vas lumen by the plug, fibrosis that occurs in and around the vas due to the presence of the plug or microinfiltration of fingers of silicone through the vas wall, or both. The mechanism of action would predict potential for reversibility of vasoc or any other formed-in-place agent. If it were not easy to remove the plugs, reversal success would likely be no better than for conventional vasectomy.

There have been no published reports of return to fertility following vasoc plug removal in humans. In this study, in most men with failed vasoc vas occlusion who subsequently had a conventional vasectomy, it was necessary to leave the plugs in place due to the extensive amount of fibrosis and tissue reaction around the occlusion site. This suggests that there was some spillage of silicone out of the vas due to leakage or rupture. Histologic exam was conducted on samples from those men where the section of the vas which included the plug was removed. In all five cases there was some silicone noted outside the lumen of the vas, with the vas appearing to be patent. Difficulties during the procedure such as multiple punctures, needle dislocation and silicone leakage had been noted during three of these five procedures. Observations made during our study suggest that at least in its current state, vasoc leads to fibrosis and tissue reaction which could make simple plug removal difficult, requiring excision and reanastomosis of the vas. There would, therefore, be no advantage over conventional vasectomy in terms of reversal.

There are a number of concerns and service delivery issues regarding vasoc vas occlusion that need to be kept in mind, even if efficacy could be improved to an acceptable level. The procedure requires specialized and costly equipment and supplies, and the complexity and technical demands of the procedure make it likely that training will be difficult. In addition, three people are required to do the vasoc vas occlusion procedure --- two to carry out the procedure and one to prepare the vasoc
and to assist with the procedure. It might be difficult for service providers not trained in vasectomy to offer vasoc vas occlusion; in 15% of men it was not possible to do the vasoc vas occlusion on one or both vasa and it was necessary to do a vasectomy. Refrigeration or freezing of one of the two components is necessary in order to keep the vasoc from curing slowly over time, and this means sites would have to have a steady supply of electricity. In many low resource settings these factors would impact on the ability of service sites to offer vasoc vas occlusion as it is currently done, even if the success rates were higher.

**CONCLUSION**

Based on the results of this study, vasoc vas occlusion is not suitable for use as a male contraceptive at this time. Not only was efficacy found to be unacceptably low, but service delivery constraints of the method in its current state would likely limit utility in low resource settings.

A safe and efficacious percutaneous occlusion method could, however, offer advantages over vasectomy, and increase the acceptability and use of contraception by men. Because such a method would be less invasive than vasectomy, it could be easier to perform, result in fewer complications, and be more acceptable to men. In addition, vas occlusion with a formed-in-place plug may be more easily reversible compared to vasectomy if simple removal of the plugs were possible.

**REFERENCES**


Acknowledgements
We would like express our appreciation to the staff of the Academic Hospital Maastricht who assisted in conducting this study; to the staff of the SCMG Clinic in Leiden, The Netherlands and Kreiskrankenhaus in Frauenfeld, Switzerland, where pre-study procedures leading to necessary instrument modifications were done; and to Willem and Emmy van Noort for technical advice and modifications to the instruments during the study. In addition, we would like to thank Evelyn Landry and David Mercer for assistance with data analysis and interpretation; Karen Beattie for comments on the draft report; and Ioanna Trilivas and Lori Leonhardt for developing the graphics for the report.