

MALE CIRCUMCISION DEVICES – STATUS AND RESEARCH UPDATE

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Sigma³ Services *Scientific & Statistical Solutions*

Outline

Male circumcision devices have potential to accelerate programme scale up

- Potentially faster, simpler procedure requiring fewer instruments
- May require less highly-trained providers
- May be more acceptable

Several devices used and well-documented in infants and boys, but safety, effectiveness, acceptability among adults in Africa not known

Devices covered

- Shang Ring, PrePex, Alis Clamp, Tara KLamp



SHANG RING



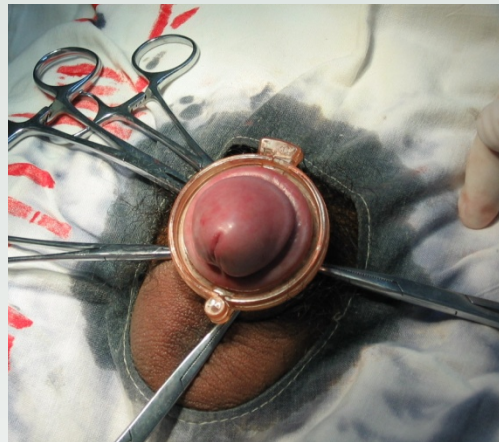
Shang Ring Device

Developed in Ningbo, China and quite extensive successful clinical use

Particular feature of everting foreskin over inner ring, placing outer ring then cutting off residual foreskin

Leaves glans exposed during healing

Device removed after 7 days



Shang Ring Clinical Data in China

Low complication rates in case series from China

0.58% bleeding, 0.67% local infection, 2.42% wound dehiscence (1200 men)

- Peng et al (*Asian J Androl.* 2008;**10**: 447–454)

0.6% bleeding, 0.6% wound infections, 0.6% wound dehiscence, 4.5% wound oedema (328 men)

- Cheng et al (*Zhonghua Nan Ke Xue.* 2009; **5**:584–592)

Infection 1.4%, mild oedema 2.6%, moderate oedema 1.4%, wound dehiscence 1.7%, no postoperative bleeding (351 men)

- Peng et al (*Zhonghua Nan Ke Xue.* 2011; **16**(11): 963-6)



Shang Ring Research, Kenya

Pilot introductory study, Homa Bay, Kenya

- 40 HIV negative men
- Device placement 4.8 (SD 2.0) minutes
- Device removal 3.9 (SD 2.6) minutes
- 6 mild adverse events (3 skin injury, 2 oedema, 1 mild infection)
- 3 partial ring detachments
- Device safe for further study in Africa
- Barone *et al.*, *JAIDS* 2011; **57**: e7



Shang Ring Research, Kenya

Healing times and spontaneous detachment, Homa Bay, Kenya

- 50 men, randomised to removal at 7, 14 or 21 days
- 22 of 35 devices for delayed removal spontaneously detached
- Seven men (14%) with partial detachment requested removal due to pain/discomfort.
- Only 1 of 20 rings in situ on Day 21
- Times to complete healing similar according to scheduled or actual removal time
- Partial detachment uncomfortable and somewhat painful
- If men do not return at 7 days, most rings will detach spontaneously by 14 days
- No serious consequences if men do not return on time for removal
- Barone et al. *JAIDS* 2012;**60**(3):e82-e89



Shang Ring Research, Kenya & Zambia

Comparison of the Shang Ring with Conventional Surgical Methods: A Randomized Controlled Trial (400 men)

- Shang Ring vs. Forceps Guided (Kenya) or Dorsal Slit (Zambia)
- Objectives/endpoints:
 - Compare pain and acceptability; compare safety and course of wound healing, including time to complete healing; compare the ease of methods
 - Compare costs; assess adherence to post-surgical instructions for wound care & sexual abstinence
- Duration of Shang Ring procedures significantly shorter at both sites (median 7 vs. 20 minutes).
- Pain at 2-day visit similar between groups at both sites.
- AEs 3% among both study groups.
- Sokal *AIDS2012* TUAC0404.



Shang Ring Research, Kenya & Zambia

A Prospective Observational Study of Male Circumcision Using the Shang Ring in Routine Clinical Settings (Field Study)

- To estimate rates of adverse events during routine service delivery, especially rare or unexpected AEs
 - Evaluate the acceptability of the Shang Ring procedure; Explore understanding of post-VMMC abstinence period and related issues; Document training methods and the cost of training; Record HIV status to evaluate whether HIV positive men are at higher risk for complications or delayed healing following Shang Ring circumcision
- Numbers: total 1200 men completing procedure (600 in each country)
- Status: Follow-up completed July 2012



Shang Ring Research, Uganda

Acceptability, safety and provider attitudes

- Self-selection to device or surgery (dorsal slit)
- 250 men choosing Shang Ring or conventional surgery (up to 1000 men, including historical controls)
- Uniform recording of healing times
- Rakai Health Sciences Program, Uganda,
- Procedures completed, follow-up still ongoing, report pending



Shang Ring Summary

Case series

- China

Safety and efficacy

- Kenya (40 initial study + 50 healing & spontaneous detachment)

Comparative studies

- RCT Kenya (100) & Zambia (100)

Field studies

- Kenya (600) & Zambia (600)
- Uganda (250)



Shang Ring: Advantages and Disadvantages

Advantages

- Minimally invasive
 - No subcutaneous tissues of penile shaft exposed
 - No haemostasis required (other than rings)
 - No suturing required for wound closure
- Shorter procedure (Peng *et al* 2008, Barone *et al* 2012, Sokal *et al* 2012)
- Low complication rates (Cheng *et al* 2009, Barone *et al* 2012, Sokal *et al* 2012)
- Easy to train providers

Disadvantages

- Multiple device sizes
- Device stays on for 7 days and requires removal visit
- Healing by secondary intention, possibly longer than for surgery



PREPEX

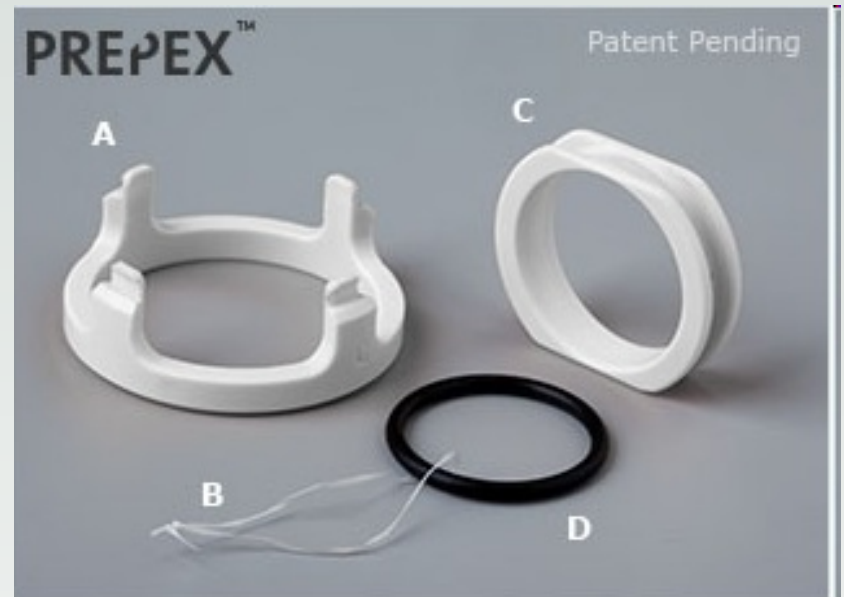


PrePex Device

- ❑ Developed in Tel Aviv, Israel with initial clinical work conducted in Rwanda
- ❑ Inner ring (C) placed between glans and foreskin
- ❑ Outer O-ring (D) applied externally to foreskin using the applicator (A) and pinches foreskin in groove in inner ring
- ❑ O-ring compresses foreskin causing ischemia
- ❑ Necrotic foreskin removed, together with device, after 7 days
- ❑ No anaesthesia required

Circ MedTech, Tel Aviv, Israel

<http://www.prepex.com/>



PrePex Device Studies, Rwanda

Initial clinical development in Rwanda

- Feasibility phase 5 men, devices removed D12 (2) and D14 (3)
- Main phase 50 men, removal D4 (5) then D7 (45)
- No anaesthesia, 1 g paracetamol at placement

Prospective randomized open label trial comparing the PrePex™ system to surgical circumcision

- 144 PrePex, 73 dorsal slit
- Low AE rates, substantially faster operation time, even if add removal time
- Healing times: PrePex 45 (SD 12.1) days vs. surgery 30 (SD 7.5) days

Open label prospective study to assess the safety and efficacy of different management methods of the PrePex circumcision device

- Compare different pain-control measures

Open label field study to assess the safety of PrePex circumcision device when performed by non-physicians

- 578 men, low complication rate, safe in hands of mid-level providers



PrePex Device, Zimbabwe

Safety study

- 53 men, completed

Randomized controlled trial

- Methods: PrePex (160), forceps guided (80)
- Objectives/endpoints:
 - Safety (Adverse events)
 - Procedure times (placement, removal)
 - Resource needs
 - Healing times (photographs)
 - Pain over first 16 h following placement and during removal
- Completed

Field Study

- 600 men, device placed and removed by nurse providers
- All procedures complete, last follow-up 16 Oct 12



PrePex Device, Uganda

Field Study

- To assess AE rates, acceptability and costs of PrePex device in comparison with conventional surgical circumcision
- 1,000 men seeking MMC choosing device circumcision
- Compared with men choosing conventional surgery (unclear if concurrent or historical controls)
- Device placed and removed by nurse providers
- Follow-ups at 7, 14, 35 and 42 days
- Conducted at International Hospital of Kampala, an established high volume MMC site using sleeve resection
- Status: ~500 men completed. Projected date last client completes all procedures not known



PrePex: Advantages and Disadvantages

Advantages

- Minimally invasive
 - No subcutaneous tissues of penile shaft exposed
 - No haemostasis required (other than rings)
 - No suturing required for wound closure
- Quick to apply and remove
- Easy to train providers
- No anaesthesia required during placement

Disadvantages

- Multiple device sizes
- Device stays on for 7 days and requires removal visit
- Healing by secondary intention, longer than for surgery
- Pain control protocol not yet optimised
- Some complaints of unpleasant smell



TARA KLAMP



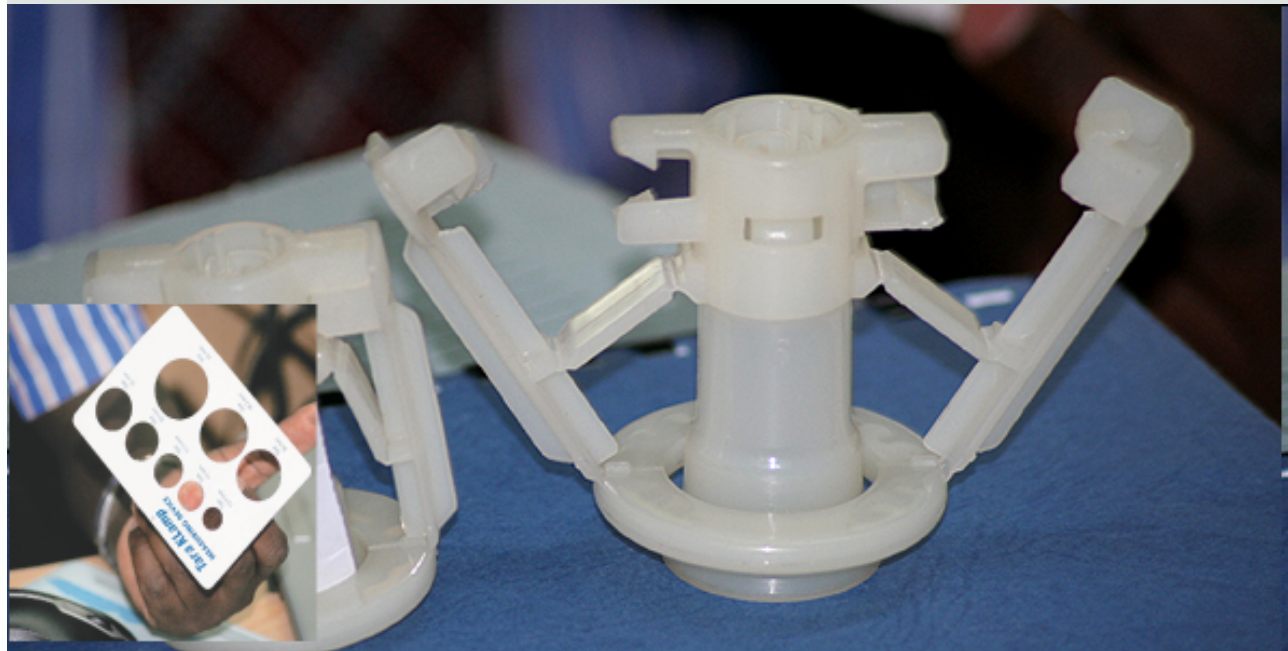
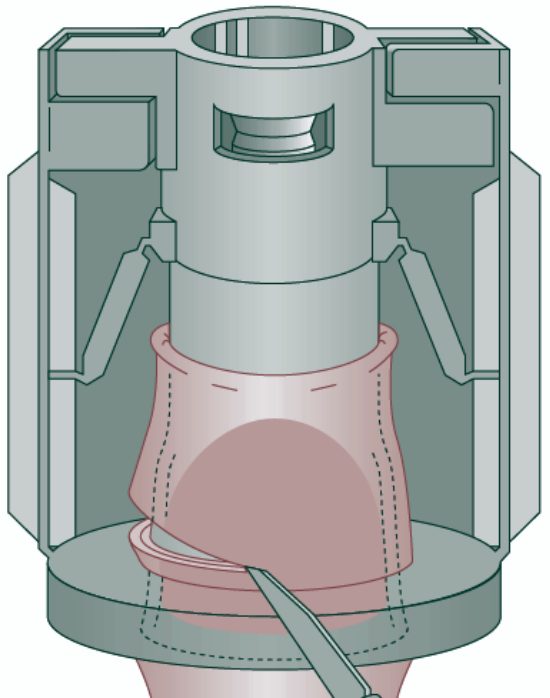
The Tara KLamp Device

<http://www.taraklamp.com/>
Taramedic Corporation, Kuala Lumpur, Malaysia

Developed by Gurcharan Singh in Malaysia

Successfully used in Malaysia for circumcision of boys, including in public sector hospitals and circumcision campaigns

Promoted by developer in Lesotho and South Africa as an improvement on existing traditional methods



Randomized Controlled Trial in Orange Farm

Men from control group in Orange Farm male circumcision trial for HIV prevention invited to participate in randomised assessment of Tara KLamp device

166 men invited, 97 declined to participate, 69 randomised Tara KLamp

- 35 men randomised
- 7 did not return, 4 switched to surgery
- 12 adverse events (sepsis, bleeding, erythema, cellulitis, tube adhering to tissue, ...)

Forceps-guided surgery

- 34 men randomised
- 6 did not return
- 0 adverse events

Retraining by manufacturer's agent did not result in improved outcomes

Lagarde *et al* (2009) *South African Medical Journal*; 99:163



Tara KLamp Circumcisions in KwaZulu Natal

Few data have emerged from KZN circumcision camps on number of circumcisions performed and complication rates

- Lack of monitoring and absence of clinical adverse event information a serious limitation
- Claims made of high acceptability and low complication rates

No further clinical studies of Tara KLamp planned



ALI'S KLAMP

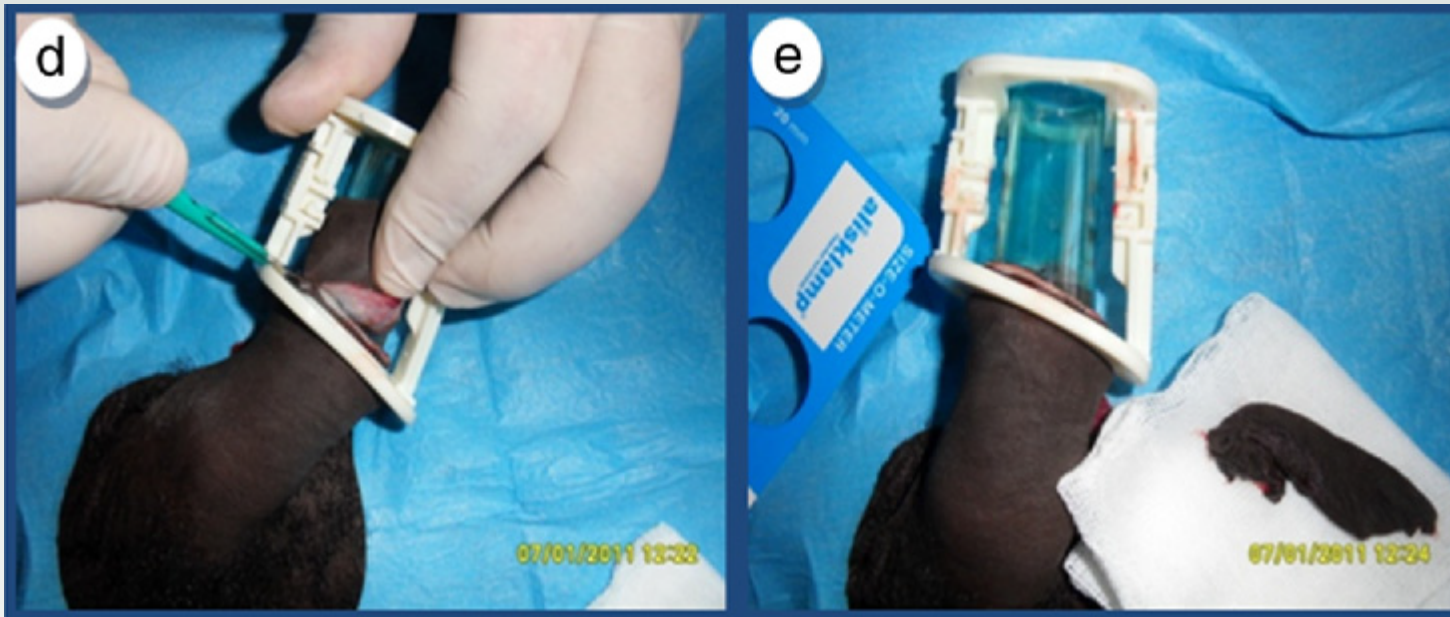


Ali's KLamp Device

Case series

- Turkey, 7,500 boys up to age 15 yr
- Turkey, 2,000 boys circumcised over 7-day period

Safety & Efficacy, Kenya, 58 men 18-45 yr



TIMELINE



Summary Timelines

Shang Ring

- Safety & Efficacy Study published 2011, 2012
- RCT and Field study results available late 2012

PrePex

- Safety & Efficacy Study published 2011
- RCT and Field Study Rwanda published 2012
- RCT Zimbabwe completed, not yet submitted to WHO
- Field Study Zimbabwe to be completed Oct 12
- Field Study Uganda ??

Alisklamp

- Safety & Efficacy Study published 2011

Tara KLamp

- Small RCT published 2009

