Development of an LMIC-adapted thermoablator

Cremer M, Alfaro K, Maza M, Garai, J, Zevallos A, Taxa L, Alonzo TA, Castle, PE, Conzuelo G, Soler M, Hilgers S, Felix J

Miriam Cremer, MD MPH
Associate Professor
Cleveland Clinic
Cleveland, OH, USA

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Disclosures

- Merck Speakers Bureau
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Cervical cancer: global burden of disease

- 4th most common cancer in women worldwide
- >528,000 new cases diagnosed every year
- >265,000 deaths in 2012
- 80% of new cases and 90% of deaths occur in low and middle income countries (LMICs)
- Primary and secondary prevention is possible

Limitations of current treatments

- Use of LEEP and CKC is limited in LMICs:
  - Require trained personnel and adequate facilities

- Cryotherapy:
  - Gas can be expensive and/or difficult to procure
  - Standard gas tank can only treat ~25 patients
  - Gas tanks are heavy, difficult to transport, pose a danger of explosion

Thermoablation as an alternative treatment

- Uses heat instead of cold to destroy tissue
- Runs on electricity (no gas required)
- In use since the 1970s in parts of the UK (more recently India, Zambia, Rwanda)
- Clinical considerations:
  - No RCT data on efficacy or safety
  - No standard treatment protocol (variations in application technique and probe tip shape, size, and temperature)

Cervix before (left) and after (right) thermoablation

Study 1

- 3-arms (N_2O gas cryotherapy vs. thermoablation vs. CryoPen®)
- Aug 2013-Jan 2015
- 64 patients aged 25-65
- Instituto Nacional de Enfermedades Neoplásicas (INEN) in Lima, Peru
- Pain assessed through a 0-10 verbal scale (0 = none, 10 = most pain)
- Outcome: depth of necrosis (3.5mm threshold)

- Thermoablation protocol:
  - 16 mm flat tip
  - 40 second application
  - 120°C

Results

	Depth of Necrosis				Pain		
	n	Range	Mean (SD)	Fail to meet 3.5 mm benchmark (%)	Range	Median	Mean (SD)
N_2O	22	3.2 – 9.1	5.5 (1.3)	1 (4.5)	1-3	1	1.5 (0.6)
CryoPen®	21	2.1 – 5.2	3.7 (0.9)	0 (0)	1-3	1	1.7 (0.8)
Thermo	21	1.5 – 6.1	3.0 (1.1)	16 (76.2)	1-6	1	3.1 (1.9)

Collaboration with WiSAP

- CryoPen® manufacturer re-designed probe tip
- Contacted WiSAP to provide the opportunity to re-design tip
- Began collaboration to create a thermoablation device adapted to LMICs
- Required features of new prototype:
  - Easily portable
  - Alternative power source (no need for electricity)
  - Simple to operate
- Meanwhile: new study using a different treatment protocol

Study 2

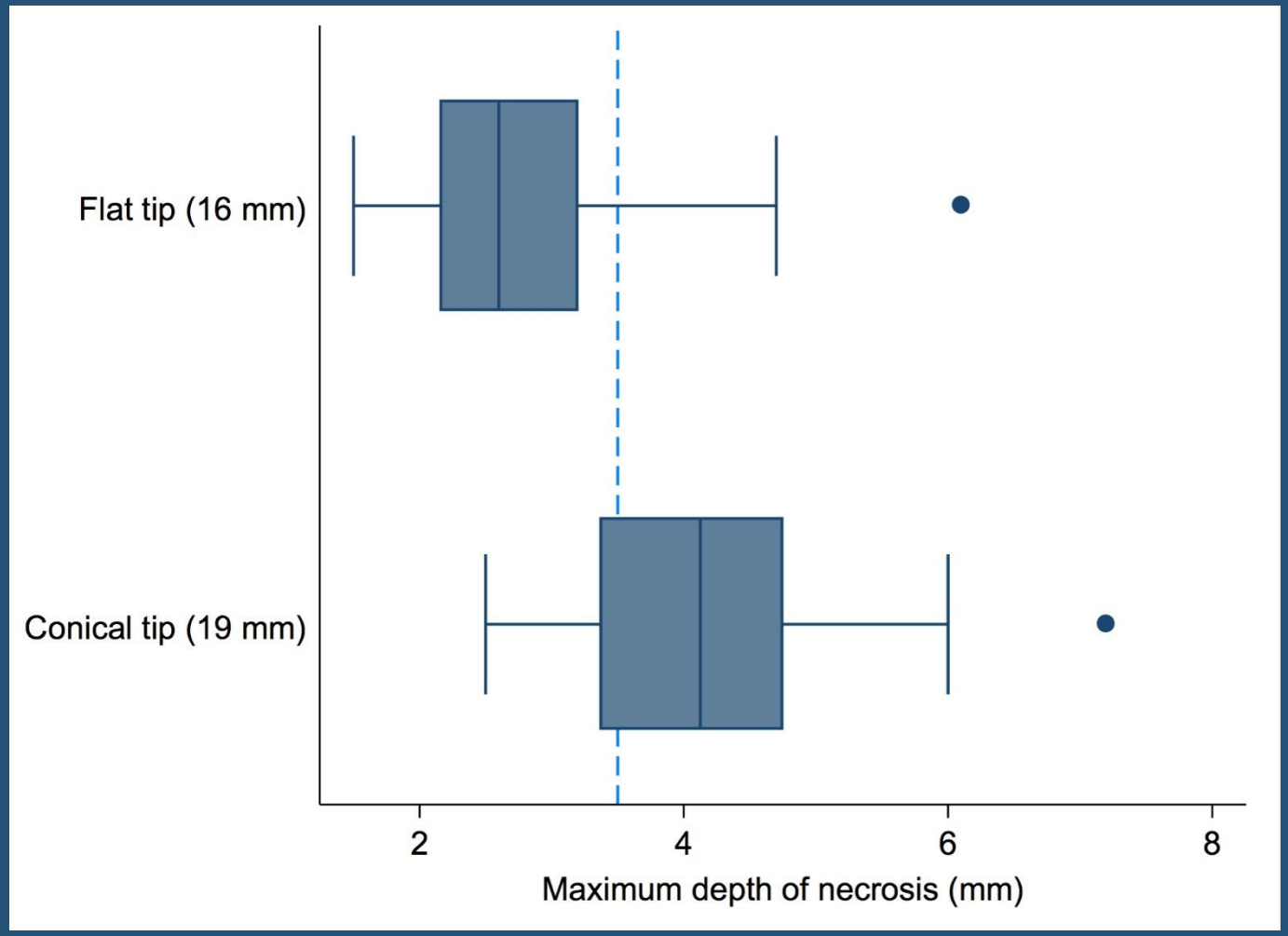
- 5-arms (CO_2 single, CO_2 double, CryoPen® single, CryoPen® double, thermoablation)
- Feb 2016-Jan 2017
- 130 patients aged 25-65 (28 thermoablation)
- Instituto Nacional de Enfermedades Neoplásicas (INEN) in Peru and Instituto Salvadoreño del Seguro Social (ISSS) in El Salvador
- Pain assessed through a 0-10 verbal scale
- Outcome: depth of necrosis (3.5mm threshold)

- Thermoablation protocol:
  - 19 mm conical tip
  - 40 second application
  - 100°C

Thermoablation results in Study 1 vs. Study 2

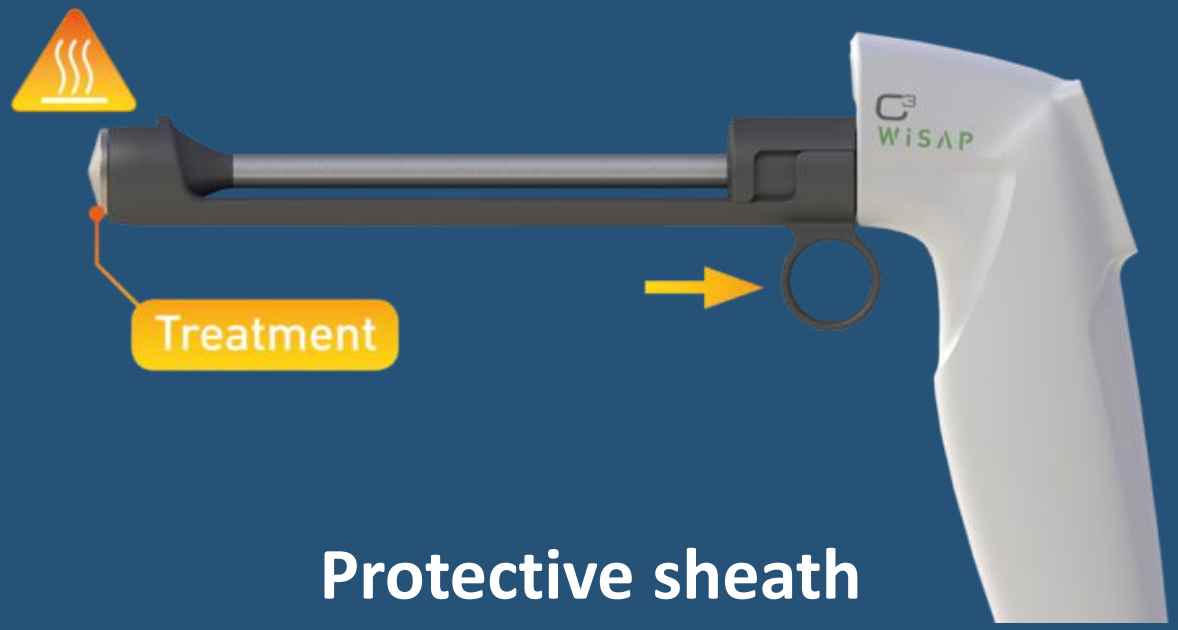
	Depth of Necrosis				Pain		
	n	Range	Mean (SD)	Fail to meet 3.5 mm benchmark (%)	Range	Median	Mean (SD)
Study 1 16mm flat	21	1.5 – 6.1	3.0 (1.1)	16 (76.2)	1-6	1	3.1 (1.9)
Study 2 19mm conical	28	2.5-7.2	4.2 (1.1)	7 (25)	1-9	3	4.0 (2.3)

Depth of necrosis comparison



Current prototype in use

Simple control panel



External rechargeable battery
(treats 100 patients per charge)

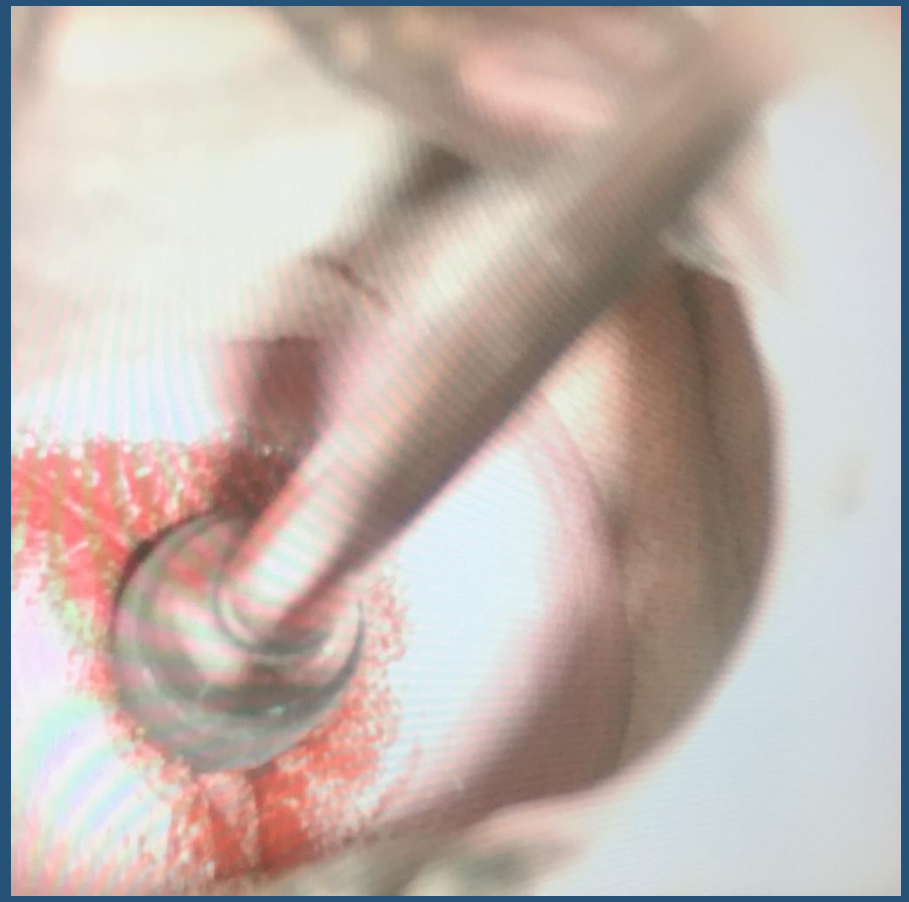
Protective sheath

Scotland Protocol/Data

- Much of the published literature is from Scotland using old WISAP device
- They use a very small tip and *enter the cervical canal* and then use a 10mm flat tip to ablate the entire TZ with multiple overlapping ablations for 20 seconds each
- They do not treat CIN2+ with conventional Cryo only large lesions with LEEP
- Large cohort of women CIN2+ treated with thermoablation
- Protocol different from LMIC devices

Thermoablation tips

Tips



Treatment

R01 study-
Single vs. Multiple tip

- 1154 women to be enrolled in Mexico
- Prototype to be developed with similar tips to old device (Arm 1)
- WISAP LMIC C3 model (Arm 2)
- CO2 based cryotherapy (Arm 3)

- First ablation 40 seconds followed by 20 second ablations to cover total TZ in arm 1 and 2
- Device to be set at 100 degrees C

Future steps

- New prototype in progress
  - Improved access and visibility

- Pain remains a concern (although reports of pain in new study are low to moderate)

- Need to standardize treatment protocol
  - Define most effective probe tip size, shape, and temperature
  - Define technique (single vs. multiple applications, location of treatment, use of different probes, etc.)

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