

Evolution of treatment options in developing countries

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Disclosures

- PATH collaborated with QIAGEN in the development and validation of the *careHPV* test.
- PATH collaborated with CryoPen, Inc. and Liger Medical, LLC in the development of new treatment devices.
- We do not receive any revenues from the commercialization of these products.
- We have not received any funding from those companies.



Background on PATH's work: Innovative screening tests and preventive treatment

careHPV™ test



OncoE6™
Cervical Test
(strip test)



Test
performance in
real-world
conditions

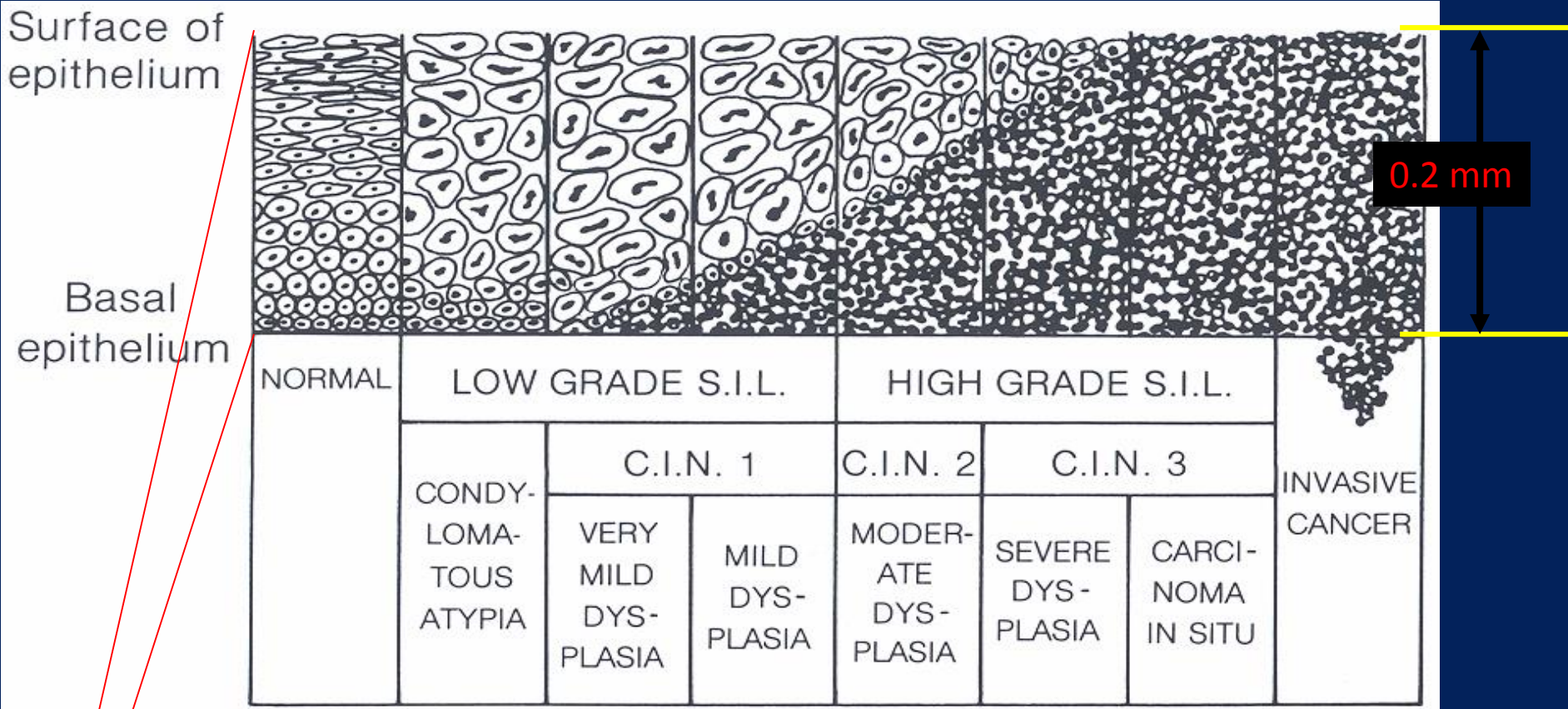


New devices for
treatment



Photos (left to right): QIAGEN; PATH/Rose Slavkovsky; PATH/Jose Jeronimo; PATH/Patrick McKern

How Deep is Deep Enough?



How Deep CIN3 goes?

	Anderson <i>et al.</i>, <i>Obstet Gynecol</i> 1980 55:546-50.	Abdul-Karim <i>et al.</i>, <i>Obstet Gynecol</i> 1982;60:210-4.
Mean Depth of CIN3	1.24 ± 0.87 mm	1.35 ± 1.15 mm
Depth of 95% of CIN3 (mean + 1.96 * SD)	2.92 mm	3.60 mm
Depth of 99.7% of CIN3 (mean + 3.00 * SD)	3.80 mm	4.80 mm



CIN3: Study in Peru

- **2.0 ± 1.3 mm** **Mean depth of CIN3**
- 4.5 mm 95% of CIN3 (mean ± 1.96 SD)
- 5.6 mm 99.7% of CIN3 (mean ± 3 SD)

Taxa y col; submitted for publication.



CIN3: Study in Peru

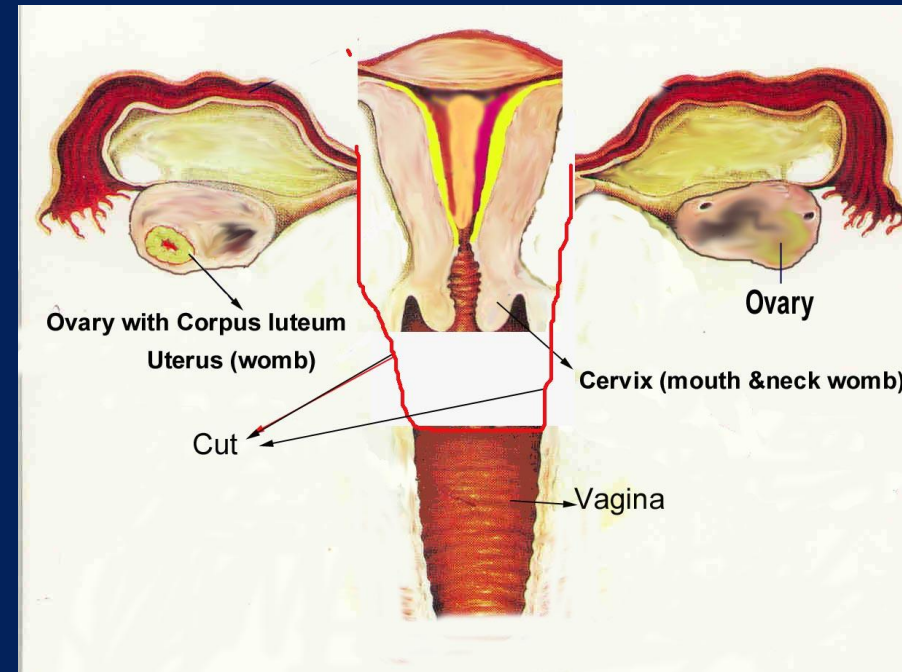
- Correlation between lineal extension and depth.
- Most lesions are very superficial.

Taxa y col; submitted for publication.



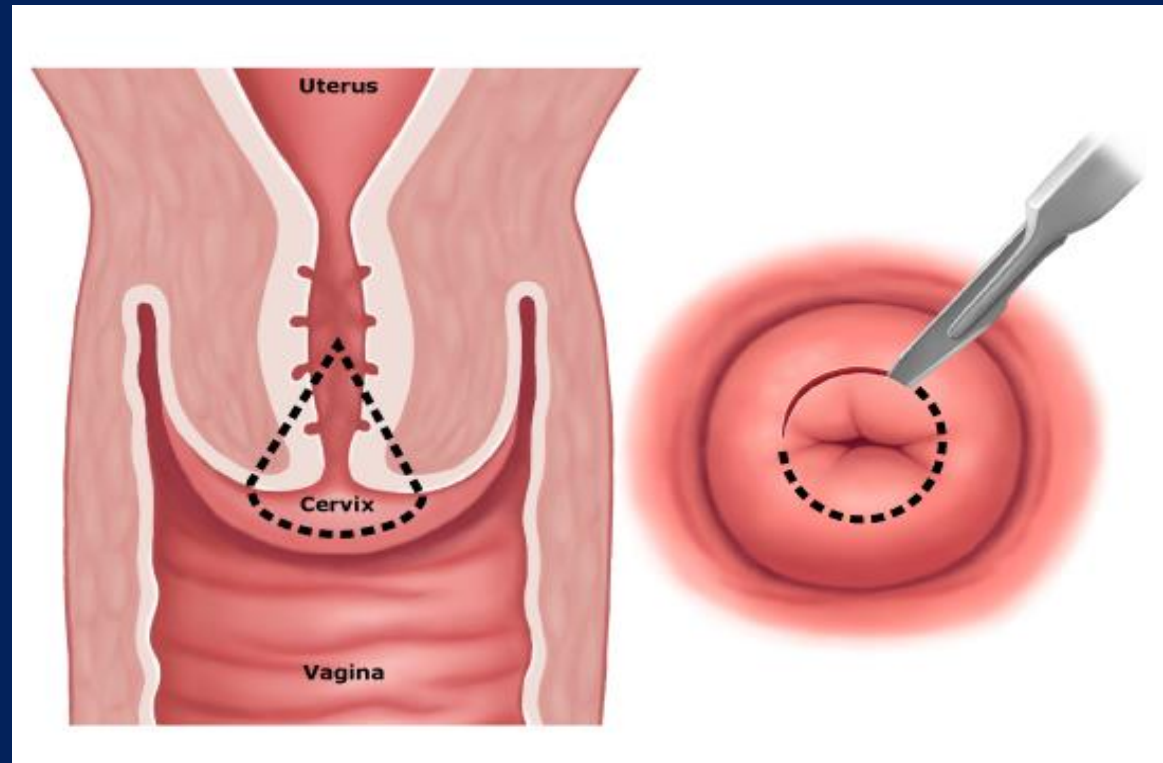
Evolution of treatment

- Hysterectomy



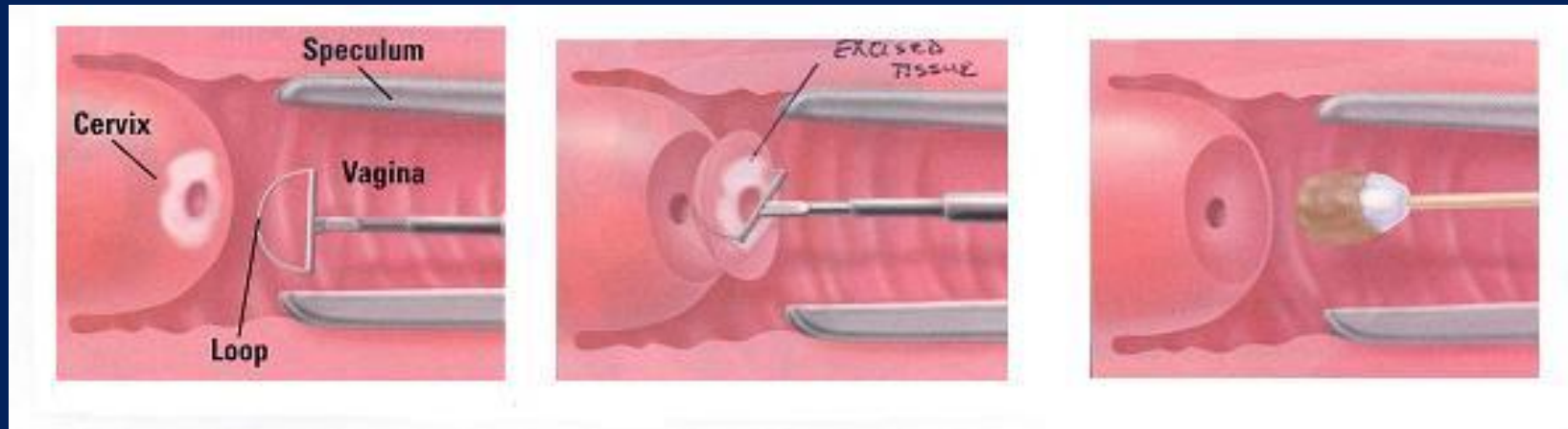
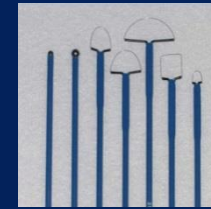
Evolution of treatment

- Hysterectomy
- **Cold Knife Cone (CKC)**



Evolution of treatment

- Hysterectomy
- Cone
- **LEEP**



LEEP in the public health systems

Role:

- Treatment of large lesions or suspicious of invasive cancer.
- Located in the referral centers.
 - Significant training required and complications

Limitations:

- Cost.
- It requires anesthesia and *electricity*.
- Need for trained personnel.
- Possibility of major complications:
 - **Bleeding.**

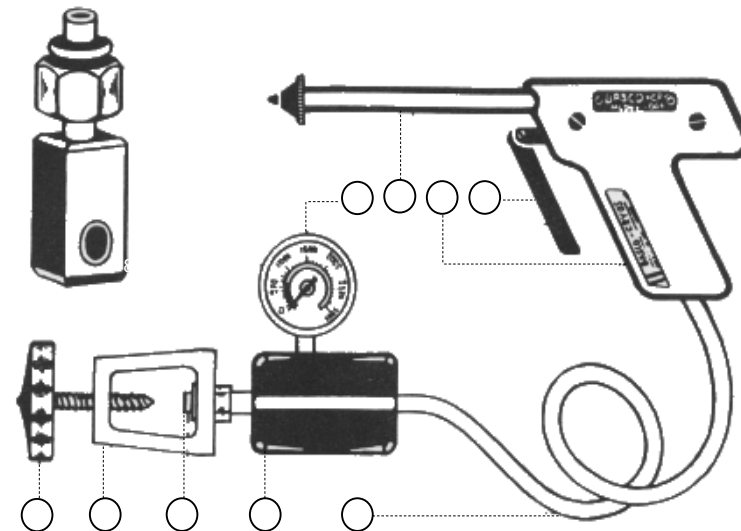
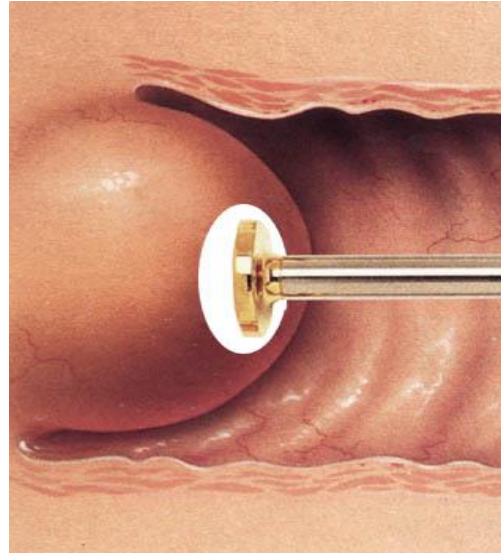


Battery-powered LEEP

- Feasible to perform 20 LEEP treatments with a fully-charged battery.
- Smoke evacuator built in the unit.
- Cost could be reduced to 2,500 dollars.
- Supply of loops would be still a problem.



Cryotherapy



Advantages of cryotherapy

- Cost.
- No need for anesthesia.
- Simple.
- Easy training.
- Technical specifications set by WHO
- Clinical recommendations by WHO document.
- Included in the UNFPA procurement system.
- No severe complications.



Effectiveness of Cryotherapy

Method	N	Failure
Cryotherapy	139	24%
Laser Vaporization	121	17%
LEEP	130	16%

[Obstet Gynecol.](#) 1998 Nov;92(5):737-44.

A randomized clinical trial of cryotherapy, laser vaporization, and loop electrosurgical excision for treatment of squamous intraepithelial lesions of the cervix.

[Mitchell MF](#)¹, [Tortolero-Luna G](#), [Cook E](#), [Whittaker L](#), [Rhodes-Morris H](#), [Silva E](#).



Effectiveness of Cryotherapy

- 531 CIN cases
- One year follow-up
- Cure: 88% any CIN
 70% for CIN3

[Int J Gynaecol Obstet.](#) 2008 May;101(2):172-7. doi: 10.1016/j.ijgo.2007.11.013. Epub 2008 Jan 22.

Effectiveness of cryotherapy treatment for cervical intraepithelial neoplasia.

[Luciani S](#)¹, [Gonzales M](#), [Munoz S](#), [Jeronimo J](#), [Robles S](#).



Limitations of cryotherapy

- Lack of technical support.
- No updated clinical recommendations at country level.
- **It needs gas supply:**



Misunderstanding developing countries

1996:

“The great advantage of cryotherapy is that it does not need electricity; it requires just gas.”



Incorporating the learnings from the last 20 years

- Not require gas or any other supply:
 - Expensive.
 - Difficult procurement system.
 - Limited number of suppliers.
 - Lack of compatibility between gas tank and cryo unit.
 - Tanks are heavy and difficult to carry for campaigns.



Gas Connectors



Temperatures reached by cryotherapy

- Testing of 4 different cryotherapy devices with N₂O and CO₂.
- With and without a gas conditioner.
- All devices reached temp. colder than -50°C with N₂O.
 - 2 devices got warmer temperatures in a proportion of N₂O tests.
- Only 2 devices reached temp. colder than -50°C with CO₂.
- Gas conditioner hindered the performance of the devices.

Winkler JL, Jeronimo J, Singreton J, Janmohamed A, Santos C. **Performance of cryotherapy devices using nitrous oxide and carbon dioxide.** Int J Gynaecol Obstet. 2010 Oct;111(1):73-7.



Timeline development of CryoPen Surgical System



CryoPen, Inc.

Demonstration of CryoPen device at PATH Seattle offices.

2012

2013

2014

2015

2016

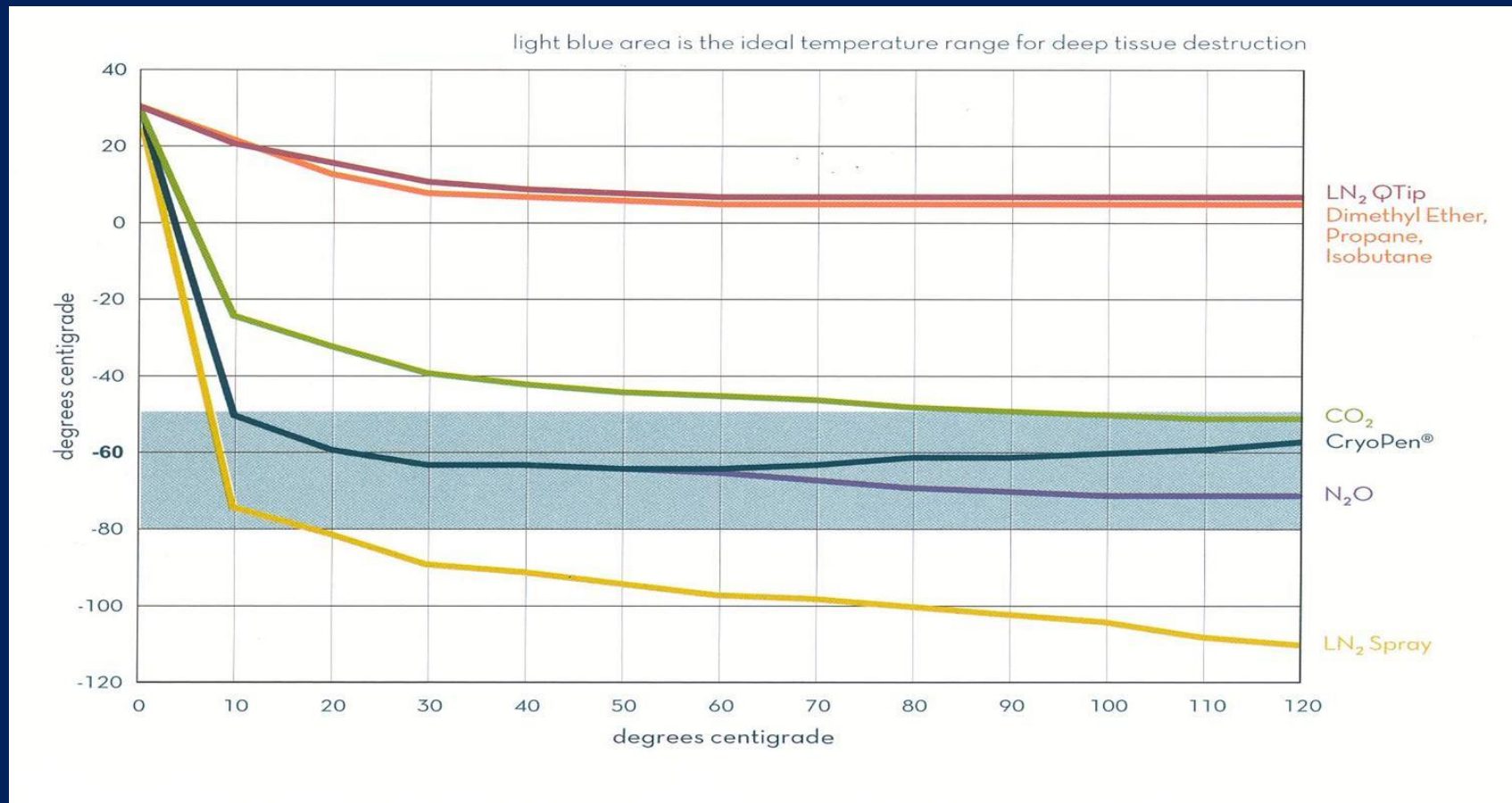


PATH carries out bench testing of CryoPen device.

PATH provides technical assistance for development of first prototype for LMIC.

CryoPen is a registered trademark of CryoPen, Inc.

CryoPen



Timeline development of CryoPen Surgical System



CryoPen, Inc.



PATH/Rose Slavkovsky

Demonstration of CryoPen device at PATH Seattle offices.

CryoPen, Inc. delivers first prototype for LMIC to PATH for evaluation.

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CryoPen



PATH/Patrick McKern



CryoPen: Characteristics

- **Portable**
 - Weight approx. 16 pounds (7.25 kg)
- **Requires electricity**
 - 1 hour for reaching optimal temperature
- **Price approx. US\$4,000 (manufacturer)**



Timeline development of CryoPen Surgical System



CryoPen, Inc.

Demonstration of CryoPen device at PATH Seattle offices.



PATH/Rose Slavkovsky

CryoPen, Inc. delivers first prototype for LMIC to PATH for evaluation.



PATH/Rose Slavkovsky

CryoPen, Inc. completes updated prototype for LMIC.

2012

2013

2014

2015

2016



PATH carries out bench testing of CryoPen device.

PATH provides technical assistance for development of first prototype for LMIC.

BHI receives NIH grant to complete development of unit for LMIC.

PATH is a project advisor.

PATH carries out field testing in Uganda.

Need for further modifications.

CryoPen: Current status

- FDA approved
- Ready for manufacturing and commercialization
 - Requires funding for expanding manufacturing capacity



PATH/Rose Slavkovsky



Exploring new alternatives: Thermal Coagulator*

- Tip heated to 120 Celsius
- It requires electricity.
- 40-second applications.



(* Formerly known as “cold-coagulator”



Cure rates using thermal coagulation

Efficacy of thermal coagulation			
Authors/Location	Year	Number treated	Efficacy
Hussein/Scotland	1985	CIN2: 21 CIN3: 33	CIN2: 95% @ 4 mo. CIN3: 85% @ 4 mo.
Singh/Singapore	1988	CIN 2/3: 47	84%
Gordon & Duncan/Scotland	1991	CIN 3: 1628	95% @ 1 yr. 92% @ 5 yrs.
Williams/England	1993	CIN2/3: 125	96.5%
Zawislak/N Ireland	2003	725 (all grades CIN)	87%



New Thermal Coagulators

- Battery-powered unit
- Multiple treatments with one fully-charged battery.
- Light incorporated
- Timer



WISAP thermal coagulators



Photos: WISAP Medical Technology GmbH



Liger Medical Thermocoagulator



PAT/Patrick McKern



PAT/Patrick McKern



Final notes

- Non-gas treatment devices are available
- Education of providers is required



PATHEM/Will Boase



Thank you



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IFCPC2017 World Congress

