PRIMO SUMMIT
MEDITERRANEO SANITÀ
Grand Hotel Oriente, Via Armando Diaz, 44 Napoli

Tavola rotonda
PRECISION MEDICINE PER UNA ONCOLOGIA SOSTENIBILE:
DALLA DIAGNOSTICA ALLA TERAPIA

Roberto Monaco, MD - Dept. Anatomical Pathology - Cardarelli Hospital - Naples (Italy)
Non-communicable Diseases (NCDs)

NCDs are the major cause of mortality globally: 2/3 of overall mortality (36/57 million), mostly due to cancer, cardiovascular disease, diabetes, chronic respiratory diseases

- Almost 80% of the mortality for NCDs occurs in middle/low-income countries; leading cause of death in most countries except in Africa (where it will materialize by 2030)
  - In middle/low-income countries people dies younger for non-communicable diseases: 29% under 60 years (13% in high-income countries)

- Non-communicable diseases have four main behavioral risk factors: tobacco use, unhealthy diet, physical inactivity, alcohol consumption

Source: Global status report on NCD 2010, WHO

High-level UN meeting on NCDs in New York, September 2011 NCD Alliance (www.ncdalliance.org)
CANCER emerges as a public health problem in low-income countries, especially in Africa.
2008
Incidence: 12.7 millions
Mortality: 7.6 millions

Prevision 2030:
Incidence: 26 millions
Mortality: 17 millions

Globocan 2012 - Cancer incidence and mortality rates related to the geographical areas
Figure 3. Most frequently diagnosed cancers worldwide, by country and sex, 2008

Most frequently diagnosed cancers, Males

Most frequently diagnosed cancers, Females

Legend:
- Lip, oral cavity
- Stomach
- Oesophagus
- Large bowel
- Liver
- Lung
- Prostate
- Kaposi sarcoma
- Bladder
- Data not available
- Not applicable
The rise of cancer in the developing world is “an impending disaster”

Developing countries do not have the resources to support an effective response to the epidemic, lacking capacity “for prevention, public education, screening and early detection, diagnosis and treatment, whether involving surgery, radiotherapy or chemotherapy,

Dr. Margaret Chan
General Director of the World Health Organization (WHO)
IAEA's Scientific Forum on 21 September 2010
Also if more than 2/3 of cancers can be prevented or treated if detected early...
The Context

In many developing countries with over-burdened health systems, cancer is a low priority in terms of allocated resources, and there are few screening or prevention programmes.

In low and middle income countries, about 70% of all cancer cases are diagnosed too late.
A major problem is the prevention of cervical cancer, the leading cause of cancer death for women in South-Western Africa, a very large region suffering also the lack of personnel able to read cytologic smears.
There is a variety of barriers for the implementation of comprehensive cytologic screening programs in low-resource settings. Perhaps the most important of these barriers is competing health needs.

Despite the importance of cervical cancer as the most common cause of cancer-related deaths in women, other health issues frequently receive a higher priority.
Poverty may be the greatest barrier to screening. Only 26% of families in sub-Saharan Africa have running water or proper sanitation facilities. In such areas, health care services are often poorly developed and focus efforts on curative, rather than preventive, health.
In this context it is necessary to increase the tools for cancer control, including diagnosis and therapy.

Therapy can not exist without a diagnosis.

The diagnosis is useful if therapy is possible.
The mission is “to potentiate SURGICAL PATHOLOGY laboratories present in developing countries or create new ones.”
In particular ...

- **Create** Histo- and Cytopathology Laboratories managed by local pathologists and local technical staff.

- **Support** education, training and updating of new local specialists

- **Train** new technicians to the preparation and reading of cytological smears (Pap smear) and to the preparation of histological slides.

- **Use** telepathology for the final diagnosis, temporarily
In Africa the lack of equipment for the management of cancer is compounded by an acute shortage of experts such as

- pathologists for diagnosis
- oncologists for treatment
- oncology nurses for care
Few Pathologists operate in Africa and vast areas of territory are devoid of Pathology Services.
“Working without pathology services means taking an educated guess about what is wrong,” he says, sanguine about the life-and-death lottery of working in a hospital in this part of Ghana, where people live on about US$ 3 a day and most cannot afford to travel for a biopsy. “We get odd kinds of tumours here because of AIDS,” he says.
Pathologists beyond the borders
Projects
The project was completed in May 2008 with the official "delivery" of the laboratory to the administrators of the Bugando Medical Center. Currently the laboratory has a medical chief (Dr Jackson Kahima) who was specialized in Uganda (Kampala) in June 2008.

The Laboratory has a workload of about 4,000 patients (cases histology) and about 1,200 cytological cases/year and hosts the practical exercises for the students of the school for biomedical laboratory technicians.
WORKLOAD AT HISTOPATHOLOGY IN Bugando Medical Centre - MWANZA TANZANIA

2010

- 3,945 Surgical cases
- 921 Cytology (FNA and Fluids)
- 251 Cervical Pap smears
AIM
The improvement of diagnostic capability in the St. Mary Lacor Hospital (Gulu District).

RESULTS
The preparation of the histocytopathology laboratory has been completed – The internal organizational procedures have been improved - Italian pathologists have started the turnover for the training of local staff – The integration of 2 specialists and the installation of a telemedicine station are planned.

Project status:
In progress
St. Mary Lacor Hospital - Gulu - Uganda

**Cytology**

- 2008: 254
- 2009: 453
- 2010: 1052

**Histology**

- 2008: 1280
- 2009: 1575
- 2010: 1930

Laboratoire di Micronucleus
CUBA

INTERVENTO
Sviluppo della diagnostica citologica nella prevenzione secondaria del carcinoma della mammella e della cervice uterina

RISULTATI
Il laboratorio è stato dotato di microscopi, un ecografo, computer, materiale didattico • È stato formato lo staff (in loco e in Italia) con conseguente miglioramento della qualità dei prelievi, dei preparati e dell’attività diagnostica.

STATO DEL PROGETTO:
CONCLUSO

<table>
<thead>
<tr>
<th></th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>31.9%</td>
<td>46.9%</td>
<td>70.2%</td>
</tr>
<tr>
<td>T3 – T4</td>
<td>21.2%</td>
<td>12.2%</td>
<td>5.4%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
</tr>
</thead>
<tbody>
<tr>
<td>Material inadeguado</td>
<td>18.8%</td>
<td>19.9%</td>
<td>6.2</td>
</tr>
<tr>
<td>Falsos positivos</td>
<td>0.8%</td>
<td>-</td>
<td>2.5%</td>
</tr>
<tr>
<td>Falsos negativos</td>
<td>2.1%</td>
<td>2%</td>
<td>1.8%</td>
</tr>
</tbody>
</table>

Ca. mammella
AIM
The creation of a Histo-Cytopathology Laboratory at Mtendere Mission Hospital in Chirundu

RESULTS
The rooms designed to host the new laboratory have been restored – The necessary technical equipment has been delivered – Two technicians have been trained, in loco and in Italy – The cytological and histological diagnostic activity has been activated – A telemedicine station with satellite connection has been installed – A cervical cancer screening is in progress

Project status: Completed
AIM
The creation of a Histo-Cytopathology Laboratory at CDS Hospital in Fianarantsoa

RESULTS
The rooms designed to host the new laboratory have been restored – The necessary technical equipment has been delivered – The training of local technical staff has begun - A cervical cancer screening, through Pap smears, is in progress.

Project status:
In progress
PALESTINA

INTERVENTO
Sostegno al servizio di anatomia patologica nella West Bank (Cisgiordania)

RISULTATI
Aricchita la dotazione tecnica del laboratorio • Introdotta la diagnostica tramite immunoistochemica • Installata una stazione di telemedicina • Migliorata l’organizzazione interna del laboratorio • Formato e completato lo staff locale

STATO DEL PROGETTO:
IN CORSO

Office of Italian Cooperation
Consulate General of Italy in Jerusalem

TECHNICAL AGREEMENT

Between
Associazione Patologi Senza Frontiere
AND
The Consulate General of Italy-Italian Cooperation Office
on Implementing A Technical Assistance Program for Breast Cancer Screening
A cost-effective approach is mandatory in limited resource contexts and research should be oriented to develop innovative and less expensive diagnostic methods.
Cytology is a diagnostic procedure with distinctive features, allowing to achieve highly specific and sensitive diagnostic evaluations with low costs and few technical resources.

Therefore cytology is a viable and effective method, especially in low-income countries, allowing an early detection of the disease, particularly in cancer disease.
The availability of professional staff able to read cytologic smears is the first step to allow an Health care system to grow.
... but it’s possible to train inexperienced people to effectively learn cytology in a short time, when professional staff (pathologists, cytologists) is not available on site?

The answer is: it’s not possible that inexperienced people learn cytology in a short time, but it’s possible to educate inexperienced people to screen pap smears recognizing suspect images to submit for a second opinion (telepathology)
Over time APOF prepared a training course in 6 modules to teach cervical cytology finalized to cancer screening.

Until now, the course was successful experimented in Zambia, Congo, Nigeria, Madagascar, with about 40 trained cytoscreeners.
A virtual classroom was created (with the support of TELESA Scientific Society) to permit a distance learning in Congo, realizing a complete train (on site and from a distance) for 7 cytoscreeners.
The “Telepathology” consists of acquisition and transmission of sample images from a local site to a remote site for diagnosis, consultation and training.

The slide is fully scanned and transmitted to a server

Expert consultants have access to the server and can read the slide for the final diagnosis.
“Pathologists beyond borders” began a project at the Mtendere Mission Hospital (MMH) in Chirundu, Zambia to build and organize a Pathology Department.
It was chosen to use Pap smear to prevent and diagnose cervical carcinoma in a region of southern Zambia with a catchment’s population of about sixty thousand people. This project involved both local staff and a large group of volunteers in Italy for a remote managing of all activities, quality control and microscopic second opinions by means of an Internet connection.
A satellite connection was established
Two local staff members, with high school diploma, were trained over a period of 8 months. At the end of the training the two technicians were able to prepare histological and cytological slides and to screen conventional Pap smears.

The two new-trained technicians passed the European aptitude test for cervical cytopathology, EFCS-QUATE (European Federation of Cytology Societies - Committee on Quality Assurance, Training and Education).
At the present time the two technicians are able to manage negative cases by themselves and to select microscopic images of all suspect or positive smears.

These static images were sent over the internet to a special website where some reviewers enrolled in the program evaluate the images.

A reviewer on duty - on a rotating base - is responsible to render the final diagnosis to MMH through the same website.
Pap smears in Chirundu (5 year)

Data from S. Guzzetti, MD - APOF

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>All cases N = 7,155</th>
<th>Women aged ≤30 N = 2,892 (40.4%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Ratio</td>
</tr>
<tr>
<td>Unsatisfactory</td>
<td>422</td>
<td>5.9%</td>
</tr>
<tr>
<td>Negative cases</td>
<td>5735</td>
<td>80.2%</td>
</tr>
<tr>
<td>Overall positive cases</td>
<td>998</td>
<td>13.9%</td>
</tr>
</tbody>
</table>

ASC-US 104 1.5% 45 1.5%
AGC 17 0.2% 2 -
L-SIL 465 6.5% 203 7.0%
ASC-H 96 1.3% 28 1.0%
H-SIL 266 3.7% 68 2.4%
SCC 47 0.7% 8 0.3%
ADENOCARCINOMA 3 - -

Cyto-histological correlations (297 cases): PPV CIN 2+: 55.6%

Data collected from 7,155 out of 7,301 (98.0%) Pap smears actually recorded onto computerized database of the MMH Department of Pathology, of which diagnoses were available.
Comparison of 1534 consecutive diagnoses of Zambian technicians with the diagnoses of reviser and their agreement

<table>
<thead>
<tr>
<th></th>
<th>UNSAT</th>
<th>NEG</th>
<th>ASCUS L-SIL</th>
<th>ASC-H H-SIL CR</th>
<th>Zambian Technicians</th>
</tr>
</thead>
<tbody>
<tr>
<td>UNSAT</td>
<td>112</td>
<td>13</td>
<td>2</td>
<td>2</td>
<td>129</td>
</tr>
<tr>
<td>NEG</td>
<td>51</td>
<td>1019</td>
<td>23</td>
<td>3</td>
<td>1096</td>
</tr>
<tr>
<td>ASCUS L-SIL</td>
<td>3</td>
<td>20</td>
<td>143</td>
<td>25</td>
<td>191</td>
</tr>
<tr>
<td>ASC-H H-SIL CR</td>
<td>3</td>
<td>4</td>
<td>17</td>
<td>94</td>
<td>118</td>
</tr>
<tr>
<td>Expert</td>
<td>169</td>
<td>1056</td>
<td>185</td>
<td>124</td>
<td>1534</td>
</tr>
</tbody>
</table>

Cohen’s K = 0.76  
Gwet’s AC1 = 0.85

Data from S. Guzzetti, MD - APOF
... and for the extravaginal cytology and histology, where a screening is not feasible by the local staff ...
The two cytotechnicians are trained to prepare cytoblocks/histoblocks and to scan slides
“Scanscope Mission” starts
The files of the scanned slides are downloaded on a dedicated server

http://83.103.77.161
In Italy the "Pathologists beyond the Borders" organize a group of volunteers pathologists as consultants on virtual slides

https://patologi.sinapto.net
and a virtual Pathology Department was born.
Telepathology can compensate for the lack of pathologists in developing countries, providing a useful diagnostic service to hospitals with surgical activity and ability to further diagnostic procedures and treatment.

The presence of local technicians specifically trained allows for a low-cost telepathology for Pap smears, a diagnostic and screening tool particularly effective in regions with high incidence of cervical cancer.
At present, with the cooperation of the Italian Society of Colposcopy (SICPCV), a Center for Prevention and Treatment of cervical cancer is working at Mtendere Mission Hospital.
PROGETTO:
Implementing cervical cancer screening in IMO State - NIGERIA
### Table 5: Age-standardized incidence rates of cervical cancer by histological type and cancer registry in Nigeria

<table>
<thead>
<tr>
<th>Cancer registry</th>
<th>Carcinoma</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No data available</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Rates per 100,000 women per year.

Data sources:
IARC, Cancer Incidence in 5 Continents, Vol IX

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### Table 6: Percentage distribution of microscopically verified cases of cervical cancer by histological type and cancer registry in Nigeria

<table>
<thead>
<tr>
<th>Cancer registry</th>
<th>Histology</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>No data available</td>
<td>Period</td>
<td>MV cases</td>
</tr>
<tr>
<td></td>
<td>Squamous</td>
<td>Adeno</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Standardized rates have been estimated using the direct method and the World population as the reference.

Accumulated number of cases during the period.

MV: Microscopically Verified.

Data sources:
IARC, Cancer Incidence in 5 Continents, Vol IX
Table 33: Estimated coverage of cervical cancer screening in Nigeria

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Population studied</th>
<th>Rural or Urban</th>
<th>N Women</th>
<th>Age range</th>
<th>Coverage (%)</th>
<th>Within the last year(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No data available</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Figure 31: Estimated coverage of cervical cancer screening in Nigeria, by age and study

No data available
Figure 26: Ten most frequent HPV types among women with invasive cervical cancer in Nigeria compared to Western Africa and the World, by histology
THIS HISTOPATHOLOGY BLOCK
WAS TODAY 18TH MAY, 2007
COMMISSIONED BY
ARC. HALIMA TAYO ALAQ
HONOURABLE MINISTER OF STATE FOR HEALTH
FEDERAL REPUBLIC OF NIGERIA.
Students Training Course Cytoscreeners
Nigeria
Patologi oltre Frontiera prepared a training course for cytoscreeners in n.6 modules.

The teachers were selected according to the CV and came from Italy, Ireland, Croatia.
An advanced interactive multimicroscope system was utilized to permit the multidirectional condivision of real and digital images.
The use of this system has not only facilitated the teaching but also had an impact on the relationship with the students, influencing their level of attention and interest.
Examples of static image acquired from whole slide scanned using the software - viewer interface that allows multiple uses of the same image
The teachers (coming from different European Countries) hold the training program on site, in subsequent volunteers turning
The students had an exam at the end of the course with a mixed italo-nigerian commission (APOF, Chief Pathologist, General Director of FMC, Health Commissioner), receiving the certificates of attendance to the training.
At the same time, together with partners and the non-profit organization S.O.Solidarietà, the training for midwives and health personnel was organized.
On 06th of June 2013, the starting of the screening was celebrated with an official ceremony.
Since the beginning of the screening to date about 3500 pap smears have been performed.

The treatments with colposcopy and LEEP have started.

At moment, the first serie of slides have been collected for a multicentric quality control.
## Pap smears in Owerri June 2013 - August 2014

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>All cases N = 1618</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
</tr>
<tr>
<td>Unsatisfactory</td>
<td>157</td>
</tr>
<tr>
<td>Negative cases</td>
<td>1264</td>
</tr>
<tr>
<td>Overall positive cases</td>
<td>197</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1618</strong></td>
</tr>
<tr>
<td>ASC-US</td>
<td>40</td>
</tr>
<tr>
<td>AGC</td>
<td>-</td>
</tr>
<tr>
<td>L-SIL</td>
<td>94</td>
</tr>
<tr>
<td>ASC-H</td>
<td>11</td>
</tr>
<tr>
<td>H-SIL</td>
<td>34</td>
</tr>
<tr>
<td>SCC</td>
<td>13</td>
</tr>
<tr>
<td>ADENOCARCINOMA</td>
<td>5</td>
</tr>
</tbody>
</table>

Data collected from 1618 out of 3531 (45,7%) Pap smears actually recorded into computerized database of the FMC Department of Pathology, of which diagnoses were available.
Comparison of 424 consecutive diagnoses of Nigerian staff with the diagnoses of reviser

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>Nigerian Cytoscreeners</th>
<th>Reviser n.1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Ratio</td>
</tr>
<tr>
<td>Unsatisfactory</td>
<td>28</td>
<td>6,6%</td>
</tr>
<tr>
<td>Negative cases</td>
<td>336</td>
<td>79,2%</td>
</tr>
<tr>
<td>Overall positive cases</td>
<td>60</td>
<td>14,1%</td>
</tr>
<tr>
<td>ASC-US</td>
<td>16</td>
<td>3,8%</td>
</tr>
<tr>
<td>AGC</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>L-SIL</td>
<td>26</td>
<td>6,1%</td>
</tr>
<tr>
<td>ASC-H</td>
<td>2</td>
<td>0,5%</td>
</tr>
<tr>
<td>H-SIL</td>
<td>15</td>
<td>3,5%</td>
</tr>
<tr>
<td>SCC</td>
<td>1</td>
<td>0,2%</td>
</tr>
<tr>
<td>ADENOCARCINOMA</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Data collected from 424 out of 3531 (12%) Pap smears actually recorded into computerized database of the FMC Department of Pathology, of which reviser diagnoses were available.
Consideration

Actions aimed at improve the health status of low resources countries with geopolitical interest should be better coordinated with the political and state authorities, in order to avoid dispersion of the cooperating forces and facilitate the work concentration in areas with possible useful implications for our Country, in the management of migration flows and in the politics depending by the welfare of the resident local population in critical areas.
Thank you!

FOR ANY IDEA, SUPPORT, PROPOSAL, DONATION, ETC.

CONTACT US

http://www.apof.eu
roberto.monaco@apof.eu

PATHOLOGISTS BEYOND THE BORDERS