

Improving women's health in low-income and middle-income countries. Part II: the needs of diagnostic imaging

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The emerging challenges in female health are especially relevant in low-income and middle-income countries, where insufficient human and logistical resources limit access to proper healthcare. These challenges are related to disease spectrum, human resources, and socioeconomic, sociocultural, infrastructural, and academic disparities [1,2]. Access to adequate healthcare is even more difficult in rural versus urban areas; for many sub-Saharan countries, greater than 80% of the population is rural.

According to WHO, two-thirds of the world population lack access to any diagnostic imaging; thus, 3.5–4.7 billion individuals are denied even basic diagnostic imaging [radiography or ultrasound (US)] [3].

Diagnostic imaging modalities include plain radiography, fluoroscopy, US, nuclear medicine (NM) examinations, CT, and MRI. Hybrid imaging examinations such as single-photon emission computed tomography/computed tomography (SPECT/CT), PET/CT or PET/MR combine and draw benefits from nuclear and cross-sectional morphologic modalities.

Choosing the proper imaging technique is crucial to maximize benefits to the patient, reduce/eliminate radiation exposure, and ensure optimal use of available financial resources, often in poor and underserved environments [4]. Protocols and referral criteria established for individual health conditions or for prevention/screening programs are usually nationally based and often not applicable to other countries, especially in low-income and middle-income regions [5]. The 'iRefer' document of the UK-Royal College of Radiologists (RCR) includes comprehensive guidelines on which diagnostic test should be used in each specific clinical setting [6]. This document, however, takes into

consideration medical equipment and resources available in a high-income country such as the UK, whereas all African countries have less than 1 MRI scanner per one million individuals versus, e.g. 14 per million scanners in Denmark [3].

The choice of examination for diagnostic imaging in female health depends on the specific clinical scenario, availability of imaging investigations and treatment options, and the risk associated with the use of ionizing radiation. Ultrasonography remains the first-line examination in most of the conditions in terms of women's health related to the breast, abdominal, and pelvic organs. Other imaging modalities tailored to specific patients' conditions serve mainly for problem solving, characterization of abnormalities seen on US, local/general staging in malignant disease, preoperative assessment, monitoring response to treatment, and surveillance of malignant disease.

Plain radiographies

Plain radiography plays a very limited role in diagnosing conditions specific for female health. Radiographies are commonly used for the initial assessment of thoracic and skeletal structures for conditions similar to male and female populations.

Mammography

Mammography is a leading technique in screening programs for breast cancer and the first-line diagnostic test in nonpalpable breast lesions. Screening programs established in many countries differ significantly in the quality of tests and time intervals between scans, from every year to one scan every 5 years. Unfortunately, many low-income countries do not have sufficient financial resources and healthcare infrastructure to support screening programs and preventive medicine [7,8].

Furthermore, the reliability and sustainability of screening programs require strict quality control programs, from purely

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technical issues (e.g. calibration of the radiographic equipment or positioning during imaging) to interpretation of the images (e.g. double reading, viewing conditions, review of previous images, evaluation of early recalls, feedback information, multidisciplinary conference, diagnostic performance indicators, continuing education). In screening programs for breast cancer, the role of the radiographer is also very important, especially for personal communication and sensitive/emotional issues.

Mammography requires adequate competence and training of dedicated personnel to guarantee high-quality diagnostic information and reduce unnecessary recalls for undetermined findings. Focus is also required on the psychological aspects experienced by apparently healthy women. Cases with doubtful mammograms can be clarified by US, MRI, and/or mammoscintigraphy (see below).

Hysterosalpingiography

Hysterosalpingiography, a second-line examination for primary and secondary infertility and recurrent miscarriages, enables visualization of the endometrial cavity and assesses the patency of the fallopian tubes. In selected cases, hysterosalpingiography can be therapeutic by unblocking fallopian tubes with injected contrast under pressure [9].

Nuclear medicine imaging

Imaging with NM is based on differential uptake/accumulation in tissues/organs of different radiolabeled compounds whose concentration reflects specific functions of such tissues/organs [10]. The pathophysiologic information provided by NM is complementary to, and synergistic with the anatomic information provided by, e.g. US, radiography, CT, and MRI. NM imaging techniques are based on either single-photon emitting radiopharmaceuticals using the conventional gamma camera or positron-emitting tracers using the more complex PET equipment. Many different radiopharmaceuticals are available, each one exploring a specific tissue/organ's function with either gamma camera or PET imaging. Operating an NM imaging facility involves a number of requisites that are not consistently available in low-income and middle-income countries [11]. These requisites include the equipment *per se* and adequate human resources, logistic infrastructures, supply and handling of radiopharmaceuticals, etc. The International Atomic Energy Agency (IAEA) promotes the development and sustainability of adequate structures for NM imaging in low-income and middle-income countries [11].

Although NM imaging plays important roles in the treatment and follow-up of breast cancer patients, its role in the initial diagnostic approach is more limited [12,13]. Indications for mammoscintigraphy with technetium (^{99m}Tc)-sestamibi using a breast-dedicated gamma camera (usually after first-line imaging with US and/or mammography) include high-risk patients with more than 20% lifetime risk for breast cancer, a family history

of breast cancer and breast cancer susceptibility protein-positive individuals, assessment of response to neoadjuvant chemotherapy, screening in the augmented breast, an patients for whom MRI would be indicated, but not possible or contraindicated [13].

The use of small-field-of-view PET scanners dedicated to the breast (or PEM) is based on the metabolic tracer ^{18}F -FDG; although its imaging performance is excellent, so far, PEM is limited to very few centers worldwide [14].

NM imaging in patients with gynecological cancers is based on ^{18}F -FDG-PET/CT [15]. Cervical cancers concentrate ^{18}F -FDG with increasing intensity from well-differentiated, less aggressive to poorly differentiated, more aggressive tumors; thus, the PET/CT findings also have prognostic value. ^{18}F -FDG-PET/CT is more sensitive than CT or MRI for detecting lymph node metastases in patients with cervical cancer, although micrometastatic involvement of lymph nodes may be missed.

Although PET/CT plays a pivotal role in assessing response to chemotherapy in patients with cervical cancer, its performance in patients with endometrial cancer is suboptimal. The intensity of ^{18}F -FDG uptake has significant prognostic value in terms of overall survival, and a PET/CT scan provides staging information that can modify the treatment strategy in over one out of five patients with newly diagnosed endometrial cancer [15].

Ultrasound imaging

US imaging, the first-line imaging examination of choice in gynecology and obstetrics, enables good visualization of the ovaries, uterus, and other pelvic organs without using ionizing radiation. In addition, US is cheap, fast, and widely available across all countries and continents. Newer US equipment is extremely compact, therefore especially useful for reaching people/patients living in remote areas with limited access to hospitals and medical equipment [16,17]. US is ideal for point-of-care use in resource-limited and financially restrained healthcare systems; in the review by Groen *et al.* [16], US significantly altered clinical management in more than 30% of patients in the low-income/middle-income countries. Nevertheless, its diagnostic accuracy is somewhat operator dependent; therefore, different levels of training and competence can affect its reliability.

Computed tomography imaging

Plain radiographies play a limited role in diagnosing pelvic disease, e.g. for characterizing calcifications of adnexal masses (fibroids, dermoid cysts, ovarian or endometrial masses, pseudomyxoma peritonei) detected by US. CT yields cross-section images with good contrast and spatial resolution, thus visualizing pelvic and abdominal organs with multiplanar and three-dimensional reconstructions. The drawbacks of CT include its overall high cost, the use of ionizing radiation, and inferior imaging properties

relative to MRI for pelvic organs. CT is used for staging malignant diseases, for active surveillance and monitoring of metastatic disease during and after treatment, and for further characterization of adnexal and uterine lesions, when MRI is not available or cannot be performed [18,19].

MRI

MRI is used to clarify indeterminate cases at mammography and/or US, as well as to detect breast cancer and for annual screening in women at high risk and in younger women. It is an excellent imaging technique also in gynecological cancers because of its high contrast and spatial resolution, good visualization of pelvic organs, and the use of nonionizing radiation. Its downsides are the relatively long scanning times and a high overall cost. MRI is useful for detailed characterization of ovarian, adnexal, and uterine lesions detected on US and for staging of endometrial, cervical, vaginal, and vulvar malignancies [20,21].

The use of MRI is also growing during pregnancy as it provides additional relevant information over US, thus facilitating perinatal counseling and management decisions. The indications for fetal MRI depend on regional differences in perinatal management, the experience of the technicians and physicians, availability of obstetrical MRI, and access to in-utero fetal surgery. MRI during the first trimester of pregnancy should be restricted to maternal indications, even if it is not associated with any known long-term sequelae (if gadolinium contrast is not used); fetal MRI is safe at up to 3.0 T during the second and third trimesters. MRI is also useful if placental implantation abnormalities are suspected. In case of placenta accreta, increta, or percreta, MRI allows for timely referral to appropriate centers for delivery [22].

Limitation of imaging services

The generally high costs of properly operating imaging services cause wide inequalities among countries worldwide as 80% of resources for radiology/imaging services are spent for 20% of the world's population. Around 50% of all radiography machines in resource-poor areas are partially or totally unusable. In sub-Saharan Africa, up to 70% of medical equipment stands idle [23]. Multiple factors must be met for a fully functional imaging department, including an adequate building, an electricity and water supply, and necessary radiation protection for patients and staff.

In a 2010 WHO survey, countries in the lowest quartile of income have ~0.25 CT scanners per million versus 44 per million in the highest quartile [3,4,24]. There is also significant disparity in the number of radiologists, e.g. one for every 400 000 of the population in East Africa, versus one radiologist per 21 000 in the UK [25], and '<http://www.who.int/gho/enf>'. The number of radiographers, sonographers, and medical physicists in developing countries is also significantly lower, concentrated mainly in cities and teaching hospitals. For patients living in resource-poor rural settings,

lengthy transportation for appropriate diagnostic studies can significantly delay treatment and result in considerably increased socioeconomic costs to an already marginalized patient population. The World Health Assembly (WHA) has accepted resolution 60.29 on 'Global Initiative on Health Technologies' to improve accessibility and availability of appropriate medical devices and technologies in the low-resource settings. The 2013 WHO Global Action Plan aimed to establish 80% availability of affordable technology and imaging by 2025 to treat non-communicable diseases [26,27].

Ongoing efforts and desirable actions to address imaging needs for women's health

One of the main goals of the IAEA Division of Human Health is to promote improvement in the quality of healthcare by offering advice to institutions and governments, and supporting the development of human resources through training courses, coordinated research projects, publications, equipment, and focus-specific meetings.

Adequate maintenance of equipment and updating qualifications of health professionals remain a major challenge in low-income countries. It is now widely recognized that US imaging is a 'must' during antenatal care, and as such, it is already largely practiced. Nevertheless, some actions should be implemented or strengthened in low-income countries to involve the ministry of high education (to make undergraduate courses obligatory), the ministry of health and medical organizations (to implement regular maintenance of equipment), experts, and seniors (for long-term plans of comprehensive training program, such as advanced second-level US).

US imaging is indeed a genuine part of the modern obstetric practice, throughout pregnancy stages, for antenatal care, diagnosis, and treatment. Proper US monitoring reduces maternal mortality throughout – including the critical perinatal period, considering that in low-income countries, motherless children are more likely to die within 1–2 years of their mother's death. The United Nations 'Millennium Development Goal (MDG) 5' aimed to improve maternal health through reduction of maternal mortality by 75% and universal access to reproductive health by 2015. However, progress in reducing maternal mortality in low-income countries and providing family planning services has been too slow to meet such targets. The increasing application of US throughout the developing world has yielded mixed results. Although some progress was made in lowering child mortality and improving maternal health, an unanticipated consequence was an increase in sex-specific abortions, therefore an overall decline toward the MDG of 'promoting sex equality and empowering women' [28].

Possible country-level actions

A paradigmatic example of how coordinated efforts could favorably impact women's health is constituted by the

Women's Health Outreach Program, a Government-funded Egyptian National Breast Cancer Screening Program [29]. Despite persisting difficulties, this program had a major impact on current practice. Recommendations drawn from this experience include the need for an integrated IAEA/WHO screening system and advice to continue initiatives for capacity-building projects in a sustainable manner and a long-term basis, with the assistance of governments of developing countries to provide information technology support. The currently low participation of several African countries in collaborative initiatives coordinated by the IAEA could be addressed by organizing local technical meetings. There is also a major need in this region to train radiologists and radiographers to overcome the lack of medical physicists, which could be addressed by developing new insights, models, and approaches. Finally, new coordinated initiatives should address the goal of strengthening multidisciplinary work, recognizing this as a major need in the African region.

Possible international-level actions

The largest international organizations/societies involved in diagnostic imaging are the UK-RCR, the International Society of Radiology (ISR), the European Society of Radiology, the North American Society of Radiology, and the American College of Radiology (ACR). They provide up-to-date, evidence-based knowledge for diagnostic imaging, define guidelines, and recommendations, standardize/harmonize the practice of clinical radiology, and provide education and training.

The RCR has recently updated their 'Recommendations for cross-sectional imaging in cancer management – carcinoma of the cervix, vagina, and vulva', 'Guidance on screening and symptomatic breast imaging', and 'US training recommendations for medical and surgical specialties,' to mention a few. The dedicated interactive website 'iRefer' addresses issues of interest to clinical radiology, including imaging of the breast and imaging in obstetrics and gynecology. Similar guidelines are available for members of the ACR and other national and international societies.

The RCR and ACR have recently developed a detailed 'Specialty training curriculum for clinical radiology,' which includes a core training-gynecology module, designed as advanced/special interest training. US training for non-radiologists includes a module for gynecological applications, designed according to a three-level system, ensuring theoretical knowledge, practical training, assessment of competencies, and continuous professional development.

The ISR, ACR, RCR, and the World Federation of Paediatric Imaging already cooperate with developing countries through outreach programs and activities, designed with different levels of involvement, dependent on individual circumstances and the setting of each individual project. A seeding international program was established in 1985, when the ISR and WHO created a radiological training center at the

Department of Radiology, Kenyatta Hospital, University of Nairobi, Kenya.

The International Radiology Community has increasingly focused on public health programs such as maternal and infant mortality, or screening in cancer programs, as many of these initiatives rely on diagnostic imaging.

Possible global-level actions

The WHO endorses and/or supports several initiatives for women's health. Among the MDGs set in the year 2000 to be achieved by the year 2015, goal no. 5 specifically states 'Reduce by three quarters, between 1990 and 2015, the maternal mortality ratio' (5.A) and 'Achieve, by 2015, universal access to reproductive health' (5.B) [28,30].

The 'Bonn Call for Action' (the outcome of a joint IAEA/WHO meeting held in Bonn in December 2012) identified 10 long-term goals to improve and enhance efforts for radiation protection (http://www.who.int/ionizing_radiation/medical_exposure/Bonn_call_action.pdf). Among others, these goals include the implementation of the principle of justification for, e.g. medical imaging procedures, optimization of radiation protection and safety, education/training of health professionals on radiation protection, development of a strategic research agenda for radiation protection and radiation safety culture in healthcare, and dissemination of global information on medical exposures and occupational exposures in medicine.

In this respect, medical radiation exposure is currently the largest contributor to the population's exposure from artificial sources (95%), almost equaling natural background to the population in the USA (NCRP report no. 10) and in other countries. On the basis of these considerations, the WHO has launched a Global Initiative on Radiation Safety in Healthcare Settings, with the goal of supporting Basic Safety Standard implementation in medical settings and focusing on public health aspects of risks versus benefits of the use of radiation in healthcare.

Within the 'Bonn Call for Action' scenario, many international organizations, nongovernmental organizations, and private associations were identified as contributors toward the overall initiatives.

Health technologies, the World Health Organization, and global collaboration

The importance of health technologies in the management continuum of the dominant causes of mortality in women should not be underestimated. Medical imaging equipment falls within the spectrum of such technologies encompassed by the first resolution on health technologies, passed by the WHA in May 2007 (WHA60.29). Through this resolution, Member States acknowledged the importance of health technologies to achieve health-related development goals, urged expansion of expertise in the field of health technologies, in particular, medical devices, and requested the

WHO to take specific actions to support Member States (http://www.who.int/medical_devices/policies/Who_resolutions/en/).

Aligned with this resolution, the Medical Devices team at the WHO works to improve availability, accessibility, affordability, safety, and quality of medical technologies such as those for medical imaging. The WHO collaborates with many stakeholders including other United Nations agencies (e.g. IAEA), Ministry of Health counterparts, Collaborating Centres, and Non-State Actors such as nongovernmental organizations toward overarching targets, and the WHO Program of Work. These include in-country radiology improvement initiatives such as completion of radiology needs assessments to guide countries in rational radiology improvement commensurate with existing infrastructure and burden of disease.

Conclusion

Gaps in and challenges to diagnostic imaging in women's health in low-income and middle-income countries include lack of adequately trained physicians, radiographers, and medical physicists, limited availability of equipment, inadequate education, delays in adopting a true multidisciplinary approach, communication problems (radiologist–clinician–patient), lack of screening programs or noncompliance of women to the screening schedule, insufficient adoption of proper justification and optimization of procedures when using ionizing radiation, and inadequate premarital screening.

Moreover, an adequate maintenance of equipment and updating qualifications of health professionals and services remains a major challenge in low-income countries. There is also an urgent need for integrated IAEA/WHO screening systems and programs to continue initiatives for capacity-building projects in a sustainable manner and on a long-term basis.

New coordinated initiatives should address the goal of strengthening multidisciplinary work, recognizing this as a major need in many countries and continents. All such actions must be based on a multidisciplinary approach and involve various partners and professional organizations, such as the Ministry of Education (to make undergraduate courses obligatory), the Ministry of Health and other medical organizations (to implement regular maintenance of equipment), experts, and seniors (for long-term plans of comprehensive training programs). In this way, countries can properly address their needs in terms of both instrumentation and operators.

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Conflicts of interest

There are no conflicts of interest.

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