Investigations and research

Oncology: the care cycle approach

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The use of medical technology to detect the presence of cancer and assess the extent of progression has come a long way in the past 20 to 30 years, with the introduction of new modalities and advances in image and data processing. Nevertheless, much of what happens in cancer care today still leaves considerable room for improvement. Before describing some of the current weaknesses in the care of cancer patients, it is illuminating to examine two examples (based on US data) that highlight the dichotomy in the change in outcomes between two cancer types over the past 20 years: breast cancer and lung cancer.

Since their peak in the mid 1980s, there has been an approximately 25% improvement in breast cancer mortality rates. In 2003 there were about 3.8 million women living who had survived the disease, with some 180,000 new cases detected each year (2007 estimate). This ratio between survivors and new cases is explained by the overall five year survival rate of about 80%. The mortality gains and strong five year survival rate arise primarily from improvements in screening, and the widespread use of X-ray mammography. Detecting the disease at an earlier stage in its progression means that therapies can be much more effective in achieving good survival outcomes and helping to reduce healthcare costs.

The figures for lung cancer present a sharp contrast. There are approximately 235,000 new cases per year (2007 estimate) but only 355,000 survivors (2003 data), reflecting a very poor 5 year survival rate of about 15%. What is more shocking is that lung cancer survival rates have not changed much over the past 20 years.

This dichotomy between breast and lung cancer correlates with the stage at which the disease is first detected: 70% (stage 1 and 2 combined) for breast cancer, but only 30% for lung cancer, where there is no approved and reimbursed screening procedure.

The care cycle

Philips has decided to address these clinical issues with a care cycle approach [1,2]. A care cycle is defined by the US Department of Health and Human Services and the American Medical Association (AMA) as follows:

“The array of health services and care settings that address health promotion, disease prevention, and the diagnosis, treatment, management, and rehabilitation of a disease, injury, and disability. Included are primary care and specialized clinical services provided in community and primary care settings, hospitals, trauma centers, and rehabilitation and long-term care facilities”[3,4].

The care cycle is a useful tool for understanding the current status of the care process for a given medical condition (Figure 1). It provides a framework for understanding clinical needs from the perspective of both patients and care givers, with the aim of improving cost-effectiveness, access, and quality of care. In conjunction with quality improvement studies, analysis of the care cycle can show the strengths and weaknesses within the healthcare continuum.
The care cycle comprises all the touch points a patient experiences as they navigate their way through a healthcare system. The journey may start with a screening procedure, or the first symptoms. Or it may be the result of a visit to a primary care physician for an annual check up followed by diagnosis and, if disease is present, staging. After that, there is selection of the appropriate therapy, followed by the therapy itself, rehabilitation and monitoring to evaluate the success of the treatment, and then surveillance and follow up to check for recurrence, or side effects that did not immediately manifest themselves after the treatment. The journey can be very daunting and complex.

In the case of cancer in the US, the average patient who receives radiation treatment makes about one hundred visits to a care giver in the twelve months following diagnosis. In their book Redefining Healthcare [5], Michael E. Porter and Elizabeth Olmsted Teisberg postulate that the only way to bring improvement to what they consider to be a broken US healthcare system is to focus on value to the patient at the medical condition level, such as lung cancer or coronary artery disease (CAD). They describe the current system as a “zero sum game” that has not produced widespread improvements in the quality and cost of delivering care, nor given more Americans access to care. They propose moving to “value-based competition” where the focus is on value for patients, with competition, medical practice and new solutions centered on medical conditions over the full cycle of care, with innovations that increase value being strongly rewarded (reimbursement).

A focus on care cycles will provide the insights needed both to compete and create new value propositions for care givers and patients. With care cycles as the framework, teams have already begun to explore where there are weaknesses and opportunities for new and improved solutions. Some examples of this are in the treatment of lung cancer and breast cancer. In the former there is no screening procedure. Such a screening system would enable high risk patient groups to be evaluated and the disease to be diagnosed at an early stage when effective therapy is still possible.

During resection for breast cancer, surgeons are operating blind as to where the disease boundaries are, because there are no real-time tools (images, dyes or sensors) to differentiate between cancer cells and healthy tissue. As a result, up to 50% of patients require subsequent additional surgery.

In prostate cancer there is no effective way to guide biopsies, so multiple biopsy samples are taken in the hope that one of them will capture cancer cells if they are present.

There are also issues common to all cancer types. Two examples are the lack of effective management of patient information over time as a patient moves around the healthcare system, and the need for a tumor tissue sample from every patient to complete diagnosis and staging.

During the course of care most cancer patients will be clinically assessed by a primary care physician, radiologist, medical oncologist, radiation oncologist, pathologist, surgeon or interventionalist. Each of these care givers collects and records various forms of information on the status of the patient and determines the appropriate next step in the care cycle. These physicians may work in different locations, departments and/or organizations, making data aggregation very challenging. The complete multi-data view of the patient’s condition over time is critical in assessing clinical status and the appropriate next step. Today, however, this record does not exist, nor do the tools a physician needs to abstract, trend, understand and compare the patient’s condition to others that would allow for evidence-based decisions.

The second weakness, common to all cancer types, is the mandatory biopsy that provides the needed tissue from the tumor to determine if it is cancerous, and provide additional staging information. The biopsy requires the insertion of a needle into the patient, and involves the challenge of absolute targeting of the tumor. In the case of the lung this needle must often pass through the lung wall with the potential side effects of a collapsed lung.

These then are some of the oncology care cycle challenges for which we at Philips are providing innovative new solutions, thereby creating new value for care givers and patients and growth for Philips. Hopefully 20 years or sooner from now we will be able to look back on these approaches to medicine and think of them in the same way that we do today for exploratory surgery.

Meeting the challenges

Many of the new imaging and data processing techniques that are expected to improve the quality of care in the coming decades are already undergoing clinical trials, or are in an advanced stage of development.

Some 30 years ago, the only imaging techniques available for the detection and staging of cancer were conventional X-ray and, to a much lesser
extent, the first steps in radionuclide imaging. Now, there is a bewildering array of imaging modalities and techniques, each with its own strengths and weaknesses.

**Disease-specific care cycles**

Some examples of disease-specific care cycles are given below.

**Breast cancer**

The (simplified) care-cycle for breast cancer is shown in Figure 2. Screening for breast cancer is typically done using mammography (Figure 3), although in recent years MRI has been recommended for patients in high risk groups. MRI not only shows the cross-sectional morphology but also functional features such as tissue perfusion and enhancement kinetics, providing greater specificity and positive predictive value, as well as sensitivity for ductal carcinoma in situ [6,7].

For diagnosis, mammography and ultrasound are the main modalities, with an important role for MRI as well. Imaging is often followed by an image-guided biopsy to do the final diagnosis. One of the problems identified in this care cycle is (especially in the USA) the large number of biopsies that turn out to be negative. This results in patient discomfort and costs that might have been avoided, e.g. by better imaging.

In staging, additional imaging modalities come into play, including bone scans, CT and PET. All of these are shown in the article by Dr. Larhs elsewhere in this issue [8]. Also in staging, lymph nodes may be dissected to examine the spread of the disease. A problem that we identified here is the difficulty of assessing the true extent of the disease. One aspect is the problem of imaging the true extent of the lesion for the surgeon, so that it can be excised with clear margins. Another aspect is proper identification. Imaging can make a difference here. In the paper by Dr. Larhs, we see an example of how PET helps to find another metastasis, which changes the stage of the cancer (Figure 4) and hence the treatment.

In later stages of the care cycle, we see additional use of imaging. During therapy, imaging may be used to assess the response to radiation or chemotherapy. During monitoring and follow-up, imaging is used to watch out for recurrence of the disease.

**Liver cancer**

The liver is a common location for neoplasms of primary and secondary origin. From the care cycle perspective, liver cancer has two important
aspects. First, primary liver cancer in the form of hepatocellular carcinoma (HCC) is one of the most frequent and most lethal primary cancers in the world, with more than 600,000 new cases per year. This ranges from approximately 15,000 new cases in the U.S. to 350,000 new cases in China [9]. Secondly, the liver is one of the most common sites for metastatic disease. Hence, secondary liver cancer is directly related to the care cycles of late-stage colorectal, breast or lung cancer, which are the most common primary sites for the spread of cancerous tissue to the liver.

In the liver cancer care cycles, the current focus of Philips lies mainly on the diagnostic and treatment stages (Figure 5). As described in the article by Coenegrachts et al. elsewhere in this issue of Medicamundi [10], it is of paramount importance to detect liver lesions at an early stage. Innovations in multiphase computed tomography, magnetic resonance and ultrasound imaging [11] make it possible to detect and classify even small lesions with higher sensitivity and specificity (Figure 6). A diagnosis that confirms the disease at an early stage allows for more treatment options and, hence, improves the chance of successful treatment [12-16].

Advanced imaging and workflow support also play a major role in the treatment itself. In recent years, the new radiological discipline of interventional oncology has emerged, which relies heavily on imaging for oncological treatments. One of the most significant examples is the transcatheter arterial chemoembolization (TACE) procedure. In this procedure, highly toxic chemoembolic drugs are injected intra-arterially via a catheter directly to the targeted tumor site.

In this issue of Medicamundi, Mikami et al. [17] and Taguchi et al. [18] describe the role of XperCT in the TACE procedure. XperCT is a novel imaging modality based on rotational angiography with a C-arm system. XperCT provides the physician with CT-like soft tissue information in the interventional suite (Figure 7). It supports the physician during all phases of the treatment since it helps to refine diagnosis and the treatment plan, and enables treatment monitoring and outcome control without further imaging sessions outside the interventional suite.

Future innovations in imaging equipment will be further aligned to the disease care cycle in order to improve imaging, ease workflow, and integrate data from the different disease phases and the multiple imaging modalities involved.
Lung cancer

With over 170,000 new cases per year, lung cancer is the second most common cancer and the most common cause for cancer-related death (over 160,000 deaths per year) in the U.S. The relative 5-year survival rate of 15% is among the lowest of all cancer types. It depends strongly on the stage at diagnosis: it rises from 2% at stage IV to 47% at stage I. However, the majority of patients are diagnosed at late stages, and by the time lung cancer becomes symptomatic, approximately 85% of patients are incurable.

This already illustrates one of the deficiencies of the present care cycle for lung cancer, namely the absence of effective screening. Currently, the use of low-dose CT for screening of lung cancer is a matter of controversy [19, 20].

A graphical representation of the care cycle is shown in Figure 8. It starts with the diagnosis of lung cancer by a biopsy or cytology, followed by a series of examinations to determine the clinical stage of the disease, including chest X-Ray and CT. The use of CAD tools for the detection of lung nodules is discussed in the article by White et al. elsewhere in this issue [21].

Based on the clinical stage, further examinations are performed to obtain more detailed information, comprising further biopsies (mainly of different lymph node sites) and a variety of...
imaging studies. In recent years, PET and in particular PET/CT, have become more and more important, not only for detection of metastatic lymph nodes or distant metastases, but also for radiation therapy planning (cf. the article by Steenbakkers et al. in this issue [22]). Matched PET and CT information allows for a much more accurate delineation of the tumor from healthy tissue (Figure 9). To check for distant metastases, mainly in the brain, spine and bones, imaging with MRI and SPECT is also performed. Whenever possible, surgery is performed. Depending on the stage and general health status, surgery is accompanied or even replaced by a combination of chemo- and radiation therapy.

For therapy monitoring and follow-up, changes in the size of the tumor or metastatic lymph nodes are assessed in given time intervals using chest CT. However, changes in tumor morphology might be delayed with respect to metabolic response to the treatment. Therefore, functional or molecular imaging is evaluated in the context of treatment monitoring [23]. The value of FDG-PET for prediction of treatment outcome is also discussed in the article of Steenbakkers et al. in this issue [22].

Colorectal cancer

Colorectal cancer is the third most common cancer worldwide and the second most common cause of cancer death in the United States [25, 26]. Most colorectal cancers arise from benign, adenomatous polyps of which some can develop into malignant tumors over the course of many years. If polyps or tumors are detected in an early stage, treatment by endoscopic or surgical removal - sometimes complemented by chemotherapy - is highly curative. Unfortunately, currently many colorectal cancers are detected when the cancer has already metastasized, mostly to the liver. At this late stage treatment becomes much more complicated and prognosis is generally poor. The care cycle for colorectal cancer is shown in Figure 10.
There are many potential screening and diagnostic methods for the detection of colorectal cancer, including the simple digital rectal exam, stool tests for fecal blood, endoscopy (sigmoidoscopy and colonoscopy) and imaging (double contrast barium enema). Lack of screening, despite the presence of available tests, is one of the major deficiencies in the current colorectal cancer care cycle.

Experimental techniques currently under development include stool tests for DNA mutations, molecular imaging and proteomics. The last-named is aimed at detecting proteins in blood or feces that may serve as biomarkers for early disease.

During the past decade virtual colonoscopy/colonography derived from CT images has matured from research to clinical practice, and is now regarded as a primary method for colon imaging to detect polyps and colorectal cancer. Virtual colonoscopy has the potential to play an important role in improving the colorectal cancer care cycle.

**Prostate cancer**

A simplified version of the care cycle that prostate cancer patients go through in developed countries is shown in Figure 12. At present, this care cycle has two major deficiencies:

- The lack of an accurate screening test, leading to missed relevant cases and large numbers of unnecessary biopsies
- The lack of a widely available and reliable method for imaging local tumors

With respect to diagnostic imaging [27], the standard modality is conventional transrectal ultrasound. While this method makes it possible to visualize the size and shape of the prostate and guide biopsies to the organ, it is only of limited value in identifying malignant foci. Magnetic resonance (MR) imaging, particularly in combination with advanced methods such as MR spectroscopy, is helpful for assessing local disease, but due to its price is not widely used. For evaluating advanced and recurrent disease, X-ray computed tomography (CT) and radionuclide bone scans are used, as well as nuclear medical imaging of radiolabeled targeted antibodies or metabolic markers such as choline.

A novel approach to imaging localized prostate cancer is being evaluated in an on-going pilot study in the Department of Urology, AMC, Amsterdam, the Netherlands [28], using a Philips iU22 ultrasound system: Contrast-enhanced ultrasound (CEUS).

CEUS is based on the visualization of perfusion and microvascularization using microbubble contrast agents. Comparison of CEUS imaging with histology obtained after removal of the prostate (Figure 13) shows that abnormal perfusion characteristics visualized by CEUS correlate with clinically relevant cancer. The results suggest that CEUS has the potential to provide a non-invasive and cost-effective way
to localize and assess malignant prostate lesions, and could thus fill one of the key current gaps in the prostate cancer care cycle.

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References


