



Medical Home for Oncology: COA Coordinating Plans to Make It Work

BY LOLA BUTCHER

he Community Oncology Alliance is bringing oncologists, insurance companies, and patients together to develop a new business model for the delivery of cancer care. Originally developed for primary care, the patient-centered medical home is an example of the "value-based" delivery models that payers are demanding. Oncology is getting special attention because of the high costs of cancer care and the widespread belief that, through changes in the way care is delivered and paid for, patients can get better care at a lower cost than insurers are now paying.

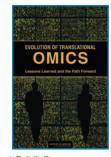
Page 8



The 'One Thing' Corporate
America Can Do to Help
Employees with Cancer p.13



Head and Neck Cancer: New Research Tackles Quality of Life p.16



New IOM Report on Best Practices for 'Omics Development p.32



Bob Young reviews Otis Brawley's New Book p.38

[ALSO]SHOP TALK.5JOE SIMONE: A Cancer Research Result to Worry About14Disclosed: Price Temple Is Paying for Fox Chase20Why Patient Navigation Needs a Process and Not Necessarily a Navigator24Meta-Analysis: Increased Risk of Death with Anti-VEGF Therapies26GEORGE SLEDGE on Recommendations27Optical Biomarkers Improve Identification of High-Risk Barrett's Esophagus35WENDY HARPHAM: Stewards of Survivorship37





Head and Neck Cancer: New Research Tackles Patient QOL



BY SARAH DIGIULIO

esearch from this year's Multidisciplinary Head and Neck Cancer Symposium focused on improving quality of life from the point of diagnosis through survivorship.

"We're curing many of these patients, which is great. But we're also realizing that with these cures, there's a lot of long-term dysfunction and morbidity that we have to deal with," said, Ezra Cohen, MD, Co-Director of the Head and Neck Cancer Program at the University of Chicago Comprehensive Cancer Center, speaking in a telephone interview after the meeting. His poster study showed that early changes in the temperature of the mucosa may be able to predict which cancer patients will develop more severe mucositis than others (Abstract #122).

Although preliminary, the findings strongly suggest that the technology used—a highly sensitive camera that can detect minuscule temperature changes to

about 0.10°C—will be an effective tool to detect the severity of this common side effect, Cohen said. "The changes would not be perceptible to the patient or physician, and we couldn't detect them with a regular thermometer or instrument."

Slight increases in mucosa temperature early in treatment were seen in patients who went on to develop the more severe cases of mucositis. The researchers analyzed 35 locally advanced head and neck (oral cavity or oropharynx) cancer patients treated with a fluorouracil- and hydroxyurea-based chemoradiotherapy regimen and took temperature measurements before treatment began, and after 15, 30, 45, and 60 Gy of radiotherapy. Higher temperatures of the mucosa early on—before and immediately following the first treatment—were associated with more severe mucositis later on.

The heat detection camera used, which was developed at Argonne National Laboratory, works by detecting infrared light and generating an electrical signal



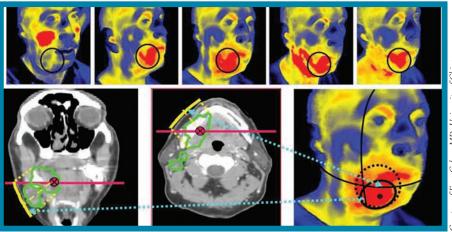
EZRA COHEN, MD: "We're curing many of these patients, which is great. But we are also now realizing that with these cures, there is a lot of long-term dysfunction and morbidity that we have to deal with."

that is then amplified and converted into digital data.

Nearly all patients with head and neck cancer treated with radiation or chemoradiation will develop some degree of mucositis, and about 60 percent develop grade 3 or 4, Cohen noted, adding that the rates of severe mucositis are increasing now that the standard treatment for this cancer type has become chemoradiation. "We accept the increased rate of toxicity because we're curing patients."

Patients with grade 3 or 4 mucositis typically need nutritional support, and sometimes gastromy tubes (if swallowing becomes too difficult) and narcotic analgesic drugs, and may need to postpone cancer treatment until symptoms lessen.

But, predicting the severity of this side effect before cancer treatment starts could make it possible for steps to be taken to start continued on page 17



This set of thermal scans of a head and neck cancer patient show temperature changes over the course of radiotherapy. The top left image was taken prior to therapy (baseline), and each image to the left was taken in subsequent two-week intervals (the second image taken two weeks into treatment, the next taken four weeks into treatment, and so on. Researchers found that increased areas of redness in the early scans (indicating higher mucosa temperatures) predicted more severe mucositis in those patients. The bottom right and center images show the radiation plan for this patient—the green outline indicates where radiation will be given.

→SIMONE

continued from page 14

becomes logarithmically more difficult. In addition, this study found that the heterogeneity problem also applied to favorable vs. unfavorable prognostic features.

As the authors calmly state, "Intratumor heterogeneity can lead to underestimation of the tumor genomics landscape portrayed from single tumor-biopsy samples and may present major challenges to personalized-medicine and biomarker development. Intratumor heterogeneity, associated with heterogeneous protein function, may foster tumor adaptation and therapeutic failure through Darwinian selection."

Cancer researchers have known about mutational evolution of cancer for some time but at least in my own simple mind, I thought it was a more deliberate process. But the life expectancy of a cancer is no longer than the human host's, so its evolutionary time frame is short; cancer is one of the most resourceful parasites on earth.

What this means for cancer therapy in general and personalized therapy specifically is not yet clear. It depends on whether this is a general phenomenon that applies, more or less, to all cancers. It also depends on the clinical significance of the mutations.

Are they all deadly? I would guess that is unlikely. Are some of the mutants sensitive to conventional therapy? I would

guess that is likely. Finally, is the extent of the observed phenomenon limited to the widely metastatic cancer stage of the four participating patients? Would we see such extreme variation in a clinically localized tumor?

What I believe to be certain if this degree of heterogeneity is found in all or many common tumors is th'e following: Clinical trials will become even more difficult or even impossible to complete using modern molecular diagnostics with current trial methods; combination therapy must be considered earlier in the drug development process.

Cancer never ceases to amaze and frustrate, and these findings continue and reinforce that effect.



ALLEN CHEN, MD: "The early quality-of-life improvements associated with IMRT not only are maintained but apparently become more magnified over time. These data provide powerful evidence attesting to the long-term benefits of IMRT for head-and-neck cancer."

may be beneficial, despite the fact that the quality of the radiation plans on paper were so much superior," said Chen, the study's lead author. "But, data such as ours, showing that IMRT significantly improves quality of life and a patient's functioning, supports its widespread

After reviewing quality-of-life scores for 155 patients previously treated with radiation therapy for locally advanced head-and-neck cancer-all of whom were disease-free and had had at least two years of follow-up—Chen and his team found scores were higher in the patients treated with IMRT (84 patients) compared with those receiving traditional conformal radiotherapy (CRT) (71 patients) and actually improved over time.

One year after treatment, the proportion of IMRT-treated patients who rated global quality of life as "very good" or "outstanding" was 51% versus 41% in CRT-treated patients. And, two years after treatment those percentages increased to 73% for IMRT-treated patients and 49% for CRT-treated patients.

IMRT allows physicians to use computerized algorithms to designate how much radiation and to define limits for the radiation delivered to a tumor. "The computer uses this trade-off model to optimize delivery of radiation so that the tumor gets the maximum amount of radiation, and the surrounding critical structures, such as the brain. salivary tissues, the eyes, and the ears, all use the minimal amount," Chen explained. "There's not a lot of conclusive evidence that the IMRT results in better curing, but these findings are demonstrating dramatic continued on page 18

→HEAD NECK CANCER

continued from page 16

treatment earlier to better support the patient. "There are chemotherapy agents that [produce a lesser] degree of mucositis. I may

"We're now learning how to pick the right regimen for the right person and further refine personalized medicine."

actually change the drug that I use concurrently with radiation to tailor the therapy to the individual patient." Cohen explained.

Next steps, he said, would be larger and prospective studies.

IMRT Radiation Technique Improves Quality of Life

Allen Chen, MD, Assistant Professor and Residency Program Director at UC Davis Cancer Center, presented findings in a poster study that intensity-modulated radiation therapy (IMRT) improved quality of life among long-term survivors of head and neck cancer based on patients' self-reports in a poster presentation. The findings

(Abstract #148) were also published in the International Journal of Radiation Oncology (doi:10.1016/j.ijrobp.2011.11.026).

"Until recently there was not a lot of clinical evidence suggesting that IMRT

Meeting Cosponsors

'he meeting is cosponsored by the American Head and Neck Society, the American Society of Clinical Oncology, the American Society for Radiation Oncology, and the Society of Nuclear Medicine.

→HEAD NECK CANCER

continued from page 17

improvements in quality of life, which really support widespread use of IMRT."

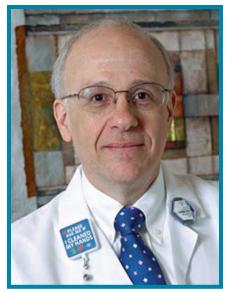
The researchers used the University of Washington Quality of Life questionnaire, which measures both health-related quality of life and global quality of life. The health-related quality-of-life measures for symptoms related to the cancer, including pain, appearance, swallowing, chewing, saliva, anxiety, and speech, and the global quality-of-life measures for both physical and mental health factors included family, friends, spirituality, and leisure activities. Using both measures was key because they reveal an overall level of global functioning, Chen said.

"Current treatments for head and neck cancer are really at the brink of tolerance levels for patients." A key takeaway message is that researchers are starting to realize that. "Even though an increasing number of patients are being cured with intensified regimens and surgery, radiation, and chemotherapy, a lot of future research will be focused on potentially identifying ways of de-intensifying treatment so that long-term function can be improved."

The most attractive reason for using IMRT therapy is the ability to spare the salivary glands, improve swallowing functions, and diminish the effects of long-term dry mouth, he said. "The data has become very clear that IMRT should become the standard of care."

Adding Chemotherapy Helps Control Some Tumor Spread

Another study (*Abstract #1*) found that adding a chemotherapy regimen to the standard of care can improve local-regional tumor control in some head and neck cancer patients—a finding that could provide a significant benefit to managing tumors in this subset of patients, said Jay Cooper, MD, Director of the Cancer Center for Maimonides Medical Center.



JAY COOPER, MD, said that at a median follow-up of 9.4 years for surviving patients with high-risk squamous cell head and neck cancer, there were no significant differences in outcome between those who did and did not receive concurrent chemotherapy and radiation.

He reported that patients whose tumors had spread from the lymph glands into the surrounding soft tissue benefited from the addition of chemotherapy at a median follow-up of more than nine years, compared with the same subgroup of patients who had received just the standard of care—i.e., surgery plus radiation therapy. But, for those patients without tumor spread into those surrounding tissues, the added chemotherapy showed no benefit.

"For two different subgroups of a population, if you treated both groups either way—either all of them got chemo or all of them didn't—that really would be ideal for the entire group," Cooper said in an interview.

Patients whose tumors
had spread from the
lymph glands into the
surrounding soft tissue
benefited from the
addition of chemotherapy
at a median followup of more than nine
years, compared with
the same subgroup
of patients who
had received just
the standard of
care of surgery plus
radiation therapy.

The initial purpose of the study, a long-term follow-up of the Radiation Therapy Oncology Group 9501/Intergroup Phase III trial, was to examine the long-term outcomes of adding chemotherapy to the standard of care. But, the researchers found that even though overall survival rates stayed relatively constant despite the added chemotherapy, certain patients (those with tumor spread in the surrounding soft tissue of the head and neck) did benefit from the addition. "This takes us a little bit further down the road of personalized therapy," he said.

The study tracked local-regional control of cancer spread in 410 high-risk resected head and neck cancer patients 10 years after treatment, separating out those who had received radiation therapy following surgery (RT: 60 Gy in 6 weeks) from those who had an identical radiation therapy regimen plus cisplatin (100 mg/m² i.v. on days 1, 22, and 43) following surgery. There was no statistical difference in overall survival between the two groups.

But in the subgroup of patients who had microscopically involved resection margins and/or extracapsular spread of disease, local regional failure was more prevalent (33%) in patients not treated with chemotherapy compared with those given cisplatin in addition to the standard surgery plus radiation (21%).



YASIR RUDHA, MD, concluded that the use of PET scanning as a routine surveillance method post-radiotherapy is a useful tool for patients with squamous cell carcinoma of the head and neck, but that it is associated with a high false-positive rate. "This should be considered when ordering radiological exams and biopsies. A negative post-therapy PET scan appears to be an excellent predictor of freedom from future loco-regional recurrence."

PET Scan Proves Valuable in Recurrence Detection

Also at the meeting, a poster study presented by Yasir Rudha, MD, of St. John Hospital/Van Elslander Cancer Center found that positron emission tomography/computed tomography (PET/CT) scans were reliable in detecting local tumor recurrence in head and neck cancer patients (*Abstract #226*).

PET scanning is a relatively new test for detecting tumor recurrence, Rudha, the study's principal investigator said in a phone interview. But, these findings suggest the scans are a reliable detection method in follow-up care for head and neck cancer patients.

He and his co-researchers, from St. John Hospital and Medical Center and St. John Macomb/Oakland Hospital, analyzed 234 head and neck cancer patients first treated with chemotherapy and radiation, and given follow-up PET/CT scans. Of the 15 positive scans, 46% were false positives and 53% were true positives. But, all of the patients with negative scans remained disease-free according to the pathological records the researchers cross-referenced to confirm their results.

Rudha said the evidence showed PET scans accurately detected negative results—if no spread was detected on the scan, no further testing is needed. But, scans that did suggest tumor spread still had the potential to be false positives, so additional tests should be recommended.

He said that positive PET results could mean non-malignant inflammatory or physiological changes, or they could mean malignancy—local regional or distant recurrence—so additional confirmation such as MRI is needed.