

3-D Ultrasound Visualizes Even Minor Fetal Defects

BY CARL SHERMAN

Contributing Writer

NEW YORK — Three-dimensional ultrasound represents an emerging advance in imaging with important applications in obstetrics, Alfred Z. Abuhamad, M.D., said at an obstetrics symposium sponsored by Columbia University and New York Presbyterian Hospital.

The ability to rotate images, change planes, and manipulate displays according

to signal strength makes it possible to visualize skeletal and vascular structures and fluid spaces, in addition to providing detailed views of fetal appearance, said Dr. Abuhamad, professor and chair of obstetrics and gynecology and director of the division of maternal-fetal medicine at Eastern Virginia Medical School, Norfolk.

The term "3-D" is something of a misnomer in that the image is displayed on a 2-D monitor. "[Instead of '3-D'] the term should be volume sonography that gives

the appearance of depth," he said. The volume image is created by the summation of 2-D slices from multiple planes, as the probe is steered from side to side.

With a multiplanar display, an image constructed from sagittal, coronal, and transverse planes can be rotated along the x-, y-, and z-axis to visualize the same structure from different angles.

The surface display shows the external aspects of the fetus, allowing the same views as in 2-D ultrasound, to review in "tremendous detail" such fetal abnormalities as clefting of the lip and palate, he said.

With "maximum mode," which manipulates the signal to enhance light (i.e. echoic) objects and dim dark (anechoic) ones, skeletal structures can be visualized, affording a look at the cranium and its fontanelles and sutures. It also facilitates assessment of bone quality and detection of fractures and permits close examination of the vertebral column.

"It's like an x-ray of the fetus," Dr. Abuhamad said.

"Minimum mode" reveals vasculature; while "inversion mode," which dims light structures and highlights dim ones, brings out fluid cavities and makes it possible to visualize such structures as the chambers of the heart and determine the number of gestational sacs, he said.

Other image manipulations permit the clinician to see the back of structures and to remove from the image, as with an "electronic scalpel," structures that may obscure features of interest.

The 3-D procedure does not use more power, increase fetal exposure, or magnify the thermal effect, compared with 2-D ultrasound, he said.

Limitations of the technique include a steep learning curve. The technique is



Absence of a T12 rib on one side in a fetus with balanced translocation was missed by 2-D ultrasound, shown by 3-D.



3-D ultrasound clearly shows swelling of the dorsal aspect of both feet in a fetus with Turner syndrome.

highly operator dependent, and the lack of standardization magnifies the possibility of human error, Dr. Abuhamad said. Also, artifacts such as motion of the woman or fetus, surface rendering, and shadowing can interfere with interpretation.

An estimated 10% of ultrasound units currently have this technology, he said. ■

Men

In two placebo-controlled, double-blind, multicenter studies in men (a two-year study of FOSAMAX 10 mg/day and a one-year study of once weekly FOSAMAX[®] [alendronate sodium] 70 mg) the rates of discontinuation of therapy due to any clinical adverse experience were 2.7% for FOSAMAX 10 mg/day vs. 10.5% for placebo, and 6.4% for once weekly FOSAMAX 70 mg vs. 8.6% for placebo. The adverse experiences considered by the investigators as possibly, probably, or definitely drug related in ≥2% of patients treated with either FOSAMAX or placebo are presented in the following table.

	Osteoporosis Studies in Men Adverse Experiences Considered Possibly, Probably, or Definitely Drug Related by the Investigators and Reported in ≥2% of Patients			
	Two-year Study		One-year Study	
	FOSAMAX 10 mg/day % (n=146)	Placebo % (n=95)	Once Weekly FOSAMAX 70 mg % (n=109)	Placebo % (n=58)
Gastrointestinal				
acid regurgitation	4.1	3.2	0.0	0.0
flatulence	4.1	1.1	0.0	0.0
gastroesophageal reflux disease	0.7	3.2	2.8	0.0
dyspepsia	3.4	0.0	2.8	1.7
diarrhea	1.4	1.1	2.8	0.0
abdominal pain	2.1	1.1	0.9	3.4
nausea	2.1	0.0	0.0	0.0

Prevention of osteoporosis in postmenopausal women

The safety of FOSAMAX 5 mg/day in postmenopausal women 40-60 years of age has been evaluated in three double-blind, placebo-controlled studies involving over 1,400 patients randomized to receive FOSAMAX for either two or three years. In these studies the overall safety profiles of FOSAMAX 5 mg/day and placebo were similar. Discontinuation of therapy due to any clinical adverse experience occurred in 7.5% of 642 patients treated with FOSAMAX 5 mg/day and 5.7% of 648 patients treated with placebo.

In a one-year, double-blind, multicenter study, the overall safety and tolerability profiles of once weekly FOSAMAX 35 mg and FOSAMAX 5 mg daily were similar.

The adverse experiences from these studies considered by the investigators as possibly, probably, or definitely drug related in ≥1% of patients treated with either once weekly FOSAMAX 35 mg, FOSAMAX 5 mg/day or placebo are presented in the following table.

	Osteoporosis Prevention Studies in Postmenopausal Women Adverse Experiences Considered Possibly, Probably, or Definitely Drug Related by the Investigators and Reported in ≥1% of Patients			
	Two/Three-Year Studies		One-Year Study	
	FOSAMAX 5 mg/day % (n=642)	Placebo % (n=648)	Once Weekly FOSAMAX 35 mg % (n=381)	Once Weekly FOSAMAX 5 mg % (n=382)
Gastrointestinal				
dyspepsia	1.9	1.4	2.2	1.7
abdominal pain	1.7	3.4	4.2	2.2
acid regurgitation	1.4	2.5	4.2	4.7
nausea	1.4	1.4	2.5	1.4
diarrhea	1.1	0.7	1.1	0.6
constipation	0.9	0.5	1.7	0.3
abdominal distention	0.2	0.3	1.4	1.1
Musculoskeletal				
musculoskeletal (bone, muscle or joint) pain	0.8	0.9	1.9	2.2

Concomitant use with estrogen/hormone replacement therapy

In two studies (of one and two years' duration) of postmenopausal osteoporotic women (total: n=853), the safety and tolerability profile of combined treatment with FOSAMAX 10 mg once daily and estrogen ± progestin (n=354) was consistent with those of the individual treatments.

Treatment of glucocorticoid-induced osteoporosis

In two, one-year, placebo-controlled, double-blind, multicenter studies in patients receiving glucocorticoid treatment, the overall safety and tolerability profiles of FOSAMAX 5 and 10 mg/day were generally similar to that of placebo. The adverse experiences considered by the investigators as possibly, probably, or definitely drug related in ≥1% of patients treated with either FOSAMAX 10 mg/day (n=157), FOSAMAX 5 mg/day (n=161), or placebo (n=159), respectively, were: **Gastrointestinal:** abdominal pain (3.2%; 1.9%; 0.0%), acid regurgitation (2.5%; 1.9%; 1.3%), constipation (1.3%; 0.6%; 0.0%), melena (1.3%; 0.0%; 0.0%), nausea (0.6%; 1.2%; 0.6%), diarrhea (0.0%; 0.0%; 1.3%); **Nervous System/Psychiatric:** headache (0.6%; 0.0%; 1.3%).

The overall safety and tolerability profile in the glucocorticoid-induced osteoporosis population that continued therapy for the second year of the studies (FOSAMAX: n=147) was consistent with that observed in the first year.

Paget's disease of bone

In clinical studies (osteoporosis and Paget's disease), adverse experiences reported in 175 patients taking FOSAMAX 40 mg/day for 3-12 months were similar to those in postmenopausal women treated with FOSAMAX 10 mg/day. However, there was an apparent increased incidence of upper gastrointestinal adverse experiences in patients taking FOSAMAX 40 mg/day (17.7% FOSAMAX vs. 10.2% placebo). One case of esophagitis and two cases of gastritis resulted in discontinuation of treatment.

Additionally, musculoskeletal (bone, muscle or joint) pain, which has been described in patients with Paget's disease treated with other bisphosphonates, was considered by the investigators as possibly, probably, or definitely drug related in approximately 6% of patients treated with FOSAMAX 40 mg/day versus approximately 1% of patients treated with placebo, but rarely resulted in discontinuation of therapy. Discontinuation of therapy due to any clinical adverse experience occurred in 6.4% of patients with Paget's disease treated with FOSAMAX 40 mg/day and 2.4% of patients treated with placebo.

Laboratory Test Findings

In double-blind, multicenter, controlled studies, asymptomatic, mild, and transient decreases in serum calcium and phosphate were observed in approximately 18% and 10%, respectively, of patients taking FOSAMAX versus approximately 12% and 3% of those taking placebo. However, the incidences of decreases in serum calcium to <8.0 mg/dL (2.0 mM) and serum phosphate to <2.0 mg/dL (0.65 mM) were similar in both treatment groups.

Post-Marketing Experience

The following adverse reactions have been reported in post-marketing use:

Body as a Whole: hypersensitivity reactions including urticaria and rarely angioedema. Transient symptoms of myalgia, malaise and rarely, fever have been reported with FOSAMAX, typically in association with initiation of treatment. Rarely, symptomatic hypocalcemia has occurred, generally in association with predisposing conditions.

Gastrointestinal: esophagitis, esophageal erosions, esophageal ulcers, rarely esophageal stricture or perforation, and oropharyngeal ulceration. Gastric or duodenal ulcers, some severe and with complications have also been reported (see WARNINGS, PRECAUTIONS, Information for Patients, and DOSAGE AND ADMINISTRATION).

Musculoskeletal: bone, joint, and/or muscle pain, occasionally severe, and rarely incapacitating (see PRECAUTIONS, Musculoskeletal Pain).

Skin: rash (occasionally with photosensitivity), pruritus, rarely severe skin reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis.

Special Senses: rarely uveitis, scleritis or episcleritis.

For more detailed information, please read the Prescribing Information.

FOSAMAX is a registered trademark of Merck & Co., Inc.



© 2005 Merck & Co., Inc., Whitehouse Station, NJ 08889, USA. All rights reserved.

20406286(1)(027)-FOS

Prenatal Exposure to Pollution May Damage Chromosomes

BY CHRISTINE KILGORE

Contributing Writer

Prenatal exposure to combustion-related air pollution may cause chromosomal abnormalities in fetal tissue, according to findings from a study of 60 New York City newborns.

In studies of other populations, such abnormalities have been linked to an increased risk of leukemia and other cancers, said Kirsti A. Bockskay of the department of environmental health sciences at Columbia University, New York, and her colleagues.

The investigators monitored exposure to polycyclic aromatic hydrocarbons (PAHs)—pollutants found in emissions from cars and other vehicles, residential heating, power generation, and tobacco smoking—among nonsmoking African American and Dominican mothers living in three low-income neighborhoods in the city.

The mothers filled out questionnaires and wore portable air monitors for 48

hours during the third trimester. Chromosomal abnormalities were measured in umbilical cord blood obtained at delivery.

The investigators found 4.7 chromosome abnormalities per 1,000 white blood cells in newborns from mothers with low exposure to PAHs and 7.2 abnormalities per 1,000 white blood cells in newborns from mothers with high exposure to PAHs.

("Low" exposure meant air pollution levels below the average, while "high" exposure referred to above-average levels).

In particular, it was stable chromosomal aberrations—not unstable aberrations—that were increased. Stable aberrations are persistent, rather than transient, markers of cytogenetic damage.

"This study has demonstrated a significant association between prenatal environmental exposure to airborne carcinogenic PAHs and stable aberrations in cord blood at the relatively low environmental concentrations found in New York City," the investigators said (Cancer Epidemiol. Biomarkers Prev. 2005;14:506-11). ■