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NOVEMBER 2013

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Charles J. Goodacre
DDS, MSD, MS

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CDA JOURNAL, VOL 41, Nº11

Jobs

BRIAN SHUE, DDS, CDE

We're No. 1. Digital media outlet *U.S. News* created "The 100 Best Jobs 2013" and ranked occupations from No. 1 to No. 100. And we're No. 1.

Dentist not only topped the best health care jobs category, but scored as the best job, period. From "The 100 Best Jobs 2013," here are the top 10 (with median salaries).[1]

1. Dentist ($142,740)
2. Registered nurse ($65,690)
3. Pharmacist ($113,390)
4. Computer systems analyst ($78,770)
5. Physician ($183,170)
6. Database administrator ($75,190)
7. Software developer ($89,280)
8. Physical therapist ($78,270)
9. Web developer ($77,990)
10. Dental hygienist ($68,500)

U.S. News, which arose from the now defunct print magazine *U.S. News and World Report*, used 2012 median salaries and jobs with the highest projected number of openings from 2010-2020 from the Bureau of Labor Statistics (BLS), U.S. Department of Labor.

Notice six of the top 10 are health care jobs while the other four are computer tech jobs. Farther down the list, dental assistant ranked No. 46 ($34,140) out of 100. Morticians didn't make the cut (population must be aging?) and neither did car salespeople (population not only aging, but driving cars longer?). Here are the bottom 10, ranked from No. 91 to No. 100: cashier ($18,820), janitor ($22,370), electrician ($49,320), delivery truck driver ($29,080), maid/housekeeper ($19,390), carpenter ($40,010), security guard ($23,900), construction worker ($29,730), fabricator ($35,170) and telemarketer ($22,520).

Notice six of the top 10 are health care jobs while the other four are computer tech jobs.

So there you have it. But before you high-five your patients, you have to realize this wasn't easy. In fact, dentist didn't make the *U.S. News* "30 Best Careers of 2009" (although hairstylists, librarians and ghostwriters did) and dentist was not even found among the "50 Best Careers in 2011" by the same media company. And although dentists ranked in the top five of 2012 Gallup Poll's most ethical professions (No. 5), it wasn't long ago that almost half of the public believed dentists did not have high ethics — not way back in the 19th century — but actually in the 1980s.

To create the best jobs list, *U.S. News* graded each job based on important factors, the most important being "median salary" (hence its heavy emphasis on dollar amounts throughout its site). It stated job seekers, regardless of the job chosen, must be able to pay for their living expenses (and smartphone data charges). The next two categories were "job prospects" and "employment rate." BLS states the unemployment rate of dentists is 0.4 percent, for example. The next level of importance was "10-year growth volume and percentage," as it doesn't bode well for job seekers if no one is hiring. The two categories given lowest importance were "stress level" and "work-life balance." Here are some stress levels as assessed by *U.S. News*: restaurant cook-above average; physician-high; telemarketer-average; dentist-average; painter-low. Work-life balance doesn't mean switching to probiotics and tofu, but to do as lyricist Neil Peart wrote, "If I could only reach that dial inside — and turn it up."

U.S. News admitted its list is subjective, but believes it can offer "potential and actual job seekers an intuitive method to compare professions based on components that matter most: the number of openings, the chance to advance and be professionally fulfilled and the ability to meet financial obligations." Notwithstanding new dentists' skyrocketing student loan debt, what can be wrong with that?

BLS reports all occupations will average a 14 percent growth from 2010 to 2020. In fact, there will be a 21 percent increase in projected dentist employment (jobs) during this period, which is an additional 27,600 general dentists and 4,600 specialists.[2] BLS holds the same 21 percent projection for oral and maxillofacial surgeons, orthodontists and prosthodontists — however, only 12 percent for other dental specialists. Additionally, dental hygienists will experience a 38 percent increase in jobs or a total of 68,500 more jobs.

But is dentistry the best job? Does *U.S. News* know about the declining caries rate, the challenges of dental benefit plans, the decline of patients wanting dental treatment (that precluded the great recession, per ADA reports) and the brewing storm known as the midlevel provider?

Step back for a moment. Remember what first brought you to this profession. Think even before you got your diploma. Go all the way back and remember the joy you experienced when your above-average DAT scores arrived in the mail. Next, think back to when you received your dental school acceptance letter(s). You were on top of the world. That feeling was indescribable. You were on your way toward becoming a dentist. It was not just going to be a job, but a passion.

Best job? I just finished a No.14-OL on a 5-year-old, who giggled during local anesthesia and stayed still during the composite restoration. The next day, a 7-year old sat in my operatory chair and said, "The drilling is the best part of the visit!"

"What do you mean," I asked. He pointed to the high-speed handpiece and said, "That's the best part. I like that!"

Those were just a few highlights from a couple of recent typical days on the job. You experience those, too. It gives true meaning to that old dental school application cliché: "I want to be a dentist because I want to help people." It doesn't get better than this. What other job or profession can give you a feeling that you are making a difference? Dentistry is truly the best out there.

And we're No. 1. ■■■■

REFERENCES

1. *U.S. News*. Best Jobs 2013. money.usnews.com/careers/best-jobs/rankings/the-100-best-jobs.
2. Bureau of Labor Statistics, U.S. Department of Labor, *Occupational Outlook Handbook, 2012-13 Edition, Dentists*. www.bls.gov/ooh/healthcare/dentists.htm. Accessed July 31, 2013.

The *Journal of the California Dental Association* welcomes letters.

We reserve the right to edit all communications and require that all letters be signed. Letters should discuss an item published in the Journal *within the past two months or matters of general interest to our readership. Letters must be no more than 500 words and cite no more than five references. No illustrations will be accepted. Letters may be submitted at editorialmanager.com/jcaldentassoc. By sending the letter to the* Journal, *the author certifies that neither the letter nor one with substantially similar content under the writer's authorship has been published or is being considered for publication elsewhere, and the author acknowledges and agrees that the letter and all rights of the author with regard to the letter become the property of the California Dental Association.*

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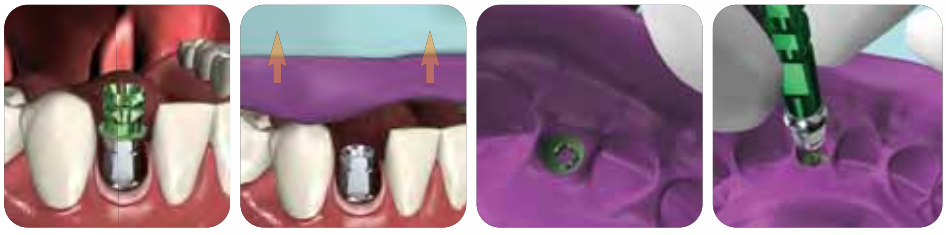

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Reputation Clipping

BY DAVID W. CHAMBERS, PHD

Have you ever wondered why dimes and quarters have little notches, called milling, around the edges? It is there to discourage clipping the coins. Back in the day, when a British pound was a pound's weight of silver, the unscrupulous filed or more aggressively clipped the edges off coins before passing them. Pretty soon, the pile of silver shavings was worth something.

That bummed out the first Queen Elizabeth who was a monetary conservative, and she proposed minting bright new money that would fairly boast of integrity. Her very shrewd financial adviser, Thomas Gresham, talked her out of it on the grounds of what has come to be known as Gresham's Law: bad money drives out good. Folks hoard the new

CONTINUES ON 803

Rise in Oral Infection Hospitalizations in U.S.

Periapical abscesses are normally managed successfully in dental practice with root canal treatment or extraction, but when left untreated, periapical abscesses can have serious consequences that can lead to hospitalization. According to a new study, there have been an increasing number of hospitalizations attributed to periapical abscesses.

In this retrospective analysis, published in the *Journal of Endodontics,* the authors used the Nationwide Inpatient Sample from 2000-2008 and selected cases with a primary diagnosis of periapical abscess with or without sinus involvement.

"During the nine-year study period, a total of 61,439 hospitalizations were primarily attributed to periapical abscesses in the United States," the authors wrote. Of these hospitalizations, 89.1 percent occurred on an emergency/urgent basis and the mean length of stay in the hospital was 2.96 days.

The number of patients hospitalized for periapical abscesses increased from 5,757 in 2000 to 8,141 in 2008, a 41.4 percent increase overall or an average annual increase of 4.6 percent, the study found.

For more information, see the full study, "Outcomes of Hospitalizations Attributed to Periapical Abscess from 2000 to 2008: A Longitudinal Trend Analysis," in the *Journal of Endodontics,* September 2013, vol. 39:9, pp. 1104-1110.

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New Clinical Recommendations: Maintain Oral Health During Pregnancy

New clinical recommendations from the American Academy of Periodontology and the European Federation of Periodontology urge expectant mothers to maintain their periodontal health as research has indicated that women with periodontal disease may be at risk of adverse pregnancy outcomes, such as giving birth to a preterm or low-birth weight baby, according to a news release from AAP.

"Tenderness, redness or swollen gums are a few indications of periodontal disease," warns Nancy L. Newhouse, DDS, MS, president of the AAP. "Other symptoms include gums that bleed with toothbrushing or eating, gums that are pulling away from the teeth, bad breath and loose teeth. These signs, especially during pregnancy, should not be ignored and may require treatment from a dental professional."

The clinical recommendations released by the AAP and the EFP state that "nonsurgical periodontal therapy is safe for pregnant women, and can result in improved periodontal health," and that it is "essential for oral health professionals (OHP) (e.g., dentists, dental hygienists, periodontists) to provide pregnant women with appropriate and timely oral health care, which includes oral health education."

"Routine brushing and flossing and seeing a periodontist, dentist or dental hygienist for a comprehensive periodontal evaluation during pregnancy may decrease the chance of adverse pregnancy complications," said Newhouse. "It is important for expectant mothers to monitor their periodontal health and to have a conversation with their periodontist or dentist about the most appropriate care. By maintaining your periodontal health, you are not only supporting your overall health, but also helping to ensure a safe pregnancy and a healthy baby."

For more information, see the supplemental article published in the *Journal of Periodontology,* 2013; vol. 84 (4 suppl.):S164-S169.

Resin Infiltration Effective on White-spot Lesions

A recent study published in the *Journal of the American Dental Association* found that resin infiltration — described by authors to be "used for restoration of teeth with interproximal incipient caries" — significantly improved the clinical appearance of enamel white-spot lesions (WSLs), an outcome of enamel demineralization.

"The reported prevalence of WSLs in orthodontic patients ranges from 4.9 percent to 97 percent, with investigators in a 2011 study reporting that 72.9 percent of patients developed a WSL during treatment," the authors wrote.

In this study, the authors split participants into a control group and a treatment group, restoring teeth with WSLs by using resin infiltration in the treatment group. They evaluated changes in WSLs photographically using a visual analog scale (VAS) and measured changes in area.

According to the authors, the results for treated teeth showed a mean reduction in WSL area of 61.8 percent immediately after treatment and 60.9 percent eight weeks later, compared with a −3.3 percent change for control teeth immediately after treatment and a 1.0 percent reduction eight weeks later.

Resin infiltration, a minimally invasive restorative treatment, significantly improved the clinical appearance of WSLs that formed during orthodontic treatment, with stable results seen eight weeks after treatment, the authors concluded.

For more information, see the study in the *Journal of the American Dental Association* September 2013, vol. 144:9, pp. 997-1005.

New Study Finds Little Evidence of Dental X-ray/Cancer Link

A recent study in the journal *Radiation Protection Dosimetry* evaluated optimized radiographic bitewing examinations to adult and juvenile patients through the use of anthropomorphic phantoms.

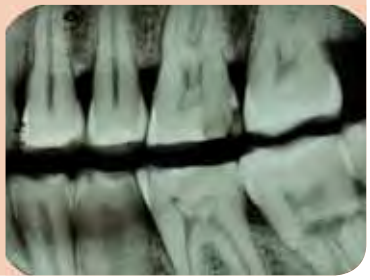
According to the authors, four anthropomorphic phantoms — an adult male, an adult female, a 10-year-old child and a 5-year-old child — were exposed to bitewing radiographs at film and digital settings using both rectangular and round collimation. Optically stimulated dosemeters were used, the study noted.

The researchers reported that for children, average organ doses were less that 40 microgray units (μGy) and the organs with the highest doses were the salivary glands, parotid, oral mucosa, skin and extrathoracic airway. For adults, the authors wrote that average organ doses were less than 200 μGy with the highest adult doses to the salivary glands, oral mucosa and skin.

Effective doses ranged from 1.5 to 1.8 micro-Sievert units (μSv) for children and from 2.6 to 3.6 μSv for adults, the authors wrote.

"Optimized doses were a fraction of the natural daily background exposure," the study noted. "Therefore, predictions of hypothetical cancer incidence or detriment in patient populations exposed to such low doses are highly speculative and should be discouraged," authors concluded.

For more information, see the full study, "Optimizing Radiographic Bitewing Examination to Adult and Juvenile Patients Through the use of Anthropomorphic Phantoms," published in *Radiation Protection Dosimetry* online first Aug. 4, 2013.



REPUTATION CLIPPING, CONTINUED FROM 801

money and circulate the old, clipped stuff.

The same is true for reputations, especially on the Internet. Everyone knows by now that slamming professionals is, for some people, a perverse passion, and for all a protected form of speech. Firms that "protect the reputations of professionals" cannot remove material from the Internet. They will advise you to have friends stuff the ballot box with nice comments, negotiate with the sites to see if you can get a placement higher on the page in exchange for "buying ads," and personally contacting grumpy customers immediately. (I would offer the same advice, and charge much less for it.)

When I was a director of a health care district board, I wanted to know more about HCAHPS (the patient satisfaction survey required by the Feds of all Medicare providers). I was interested in learning about the validity of the data collection system. For example, I wanted to see whether patients who said they had been fully informed about post-discharge routines had lower readmissions rates. Or do those who like the food live longer? My Internet search came up empty. I contacted the national firm that contracts to provide these data to most hospitals (Press Ganey) and found that they could only demonstrate reliability (patients answer consistently) and face validity (the questions look like they measure the right thing). No one seemed to understand the difference between answers that are consistent with other answers (reliability) and answers that related to health outcomes (validity). To the best of my knowledge there are no construct or predictive validity studies relating patient satisfaction to health outcomes for HCAHPS.

Gresham's Law guarantees that professionals will have their reputations clipped. There are two reasons. First, bad news travels better than good news. Righteous indignation is now a national pastime and our leaders in Washington are setting the example. Second, dentists are really very, very good at what they do. It is not news to be treated with safe, effective, health-enhancing techniques as well as respect and grace.

The nub:

1. No news is good news. Outstanding care is the norm.
2. Do not try to change people's minds; shape them at the beginning, especially while they are in your office.
3. Never circulate clipped coins or reputations.

David W. Chambers, PhD, is professor of dental education, Arthur A. Dugoni School of Dentistry, San Francisco, and editor of the Journal of the American College of Dentists.

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Study Finds Gum Disease Bacteria Facilitates Progression of Arthritis

In a new study, researchers have discovered that the bacteria responsible for gum disease facilitates the development and progression of rheumatoid arthritis.

Published in the journal *PLOS Pathogens*, researchers uncover how the bacterium responsible for periodontal disease, *Porphyromonas gingivalis* worsens rheumatoid arthritis by leading to earlier onset, faster progression and greater severity of the disease, including increased bone and cartilage destruction.

Although researchers and clinicians have long known about an association between the two prevalent chronic inflammatory diseases — periodontal disease and RA — the microbiological mechanisms have remained unclear, according to a news release from the University of Louisville School of Dentistry.

In this study, the research team found that *P. gingivalis* produces a unique enzyme, peptidylarginine deiminase (PAD) which then enhances collagen-induced arthritis (CIA), a form of arthritis similar to RA produced in the lab. PAD changes residues of certain proteins into citrulline, and the body recognizes citrullinated proteins as intruders, leading to an immune attack. In RA patients, the subsequent result is chronic inflammation responsible for bone and cartilage destruction within the joints.

"Taken together, our results suggest that bacterial PAD may constitute the mechanistic link between *P. gingivalis* periodontal infection and rheumatoid arthritis, but this ground-breaking conclusion will need to be verified with further research," said researcher Jan Potempa, PhD, DSc, of the University of Louisville School of Dentistry Oral Health and Systemic Diseases.

For more information, see the study in *PLOS Pathogens,* published online Sept. 12, 2013.

Study: Prevalence of Dentine Hypersensitivity and Associated Factors

In a recent European population-based cross-sectional study, authors evaluated the prevalence of dentine hypersensitivity and the relative importance of risk factors. They found that, overall, the prevalence of dentine hypersensitivity was high compared to many other studies, with a strong, progressive relationship between dentine hypersensitivity and erosive tooth wear.

In this study, published in the *Journal of Dentistry,* dentine hypersensitivity was clinically evaluated by cold air tooth stimulation, patient pain rating (yes or no) and investigator pain rating. Additionally, erosive tooth wear and gingival recession was recorded and patients were asked to complete a questionnaire, giving information about their dentine hypersensitivity, erosive dietary intake and toothbrushing habits.

According to the authors, 41.9 percent of patients reported pain on tooth stimulation and significant associations were found between clinically elicited dentine hypersensitivity and erosive tooth wear and gingival recession.

The questionnaire also showed "marked associations between DH and risk factors including heartburn/acid reflux, vomiting, sleeping medications, energy drinks, smoking and acid dietary intake," the study noted.

It is important to recognize the relationship between dentine hypersensitivity and erosive tooth wear for patient preventive therapies and clinical management of associated pain, the authors concluded.

For more information, see the study in the *Journal of Dentistry,* published online Aug. 5, 2013.

Study Finds Head and Neck Surgeons in Support of HPV Vaccinations

A recent study, which aimed to assess the knowledge and beliefs of head and neck surgeons regarding HPV education and vaccination, has found that these surgeons are knowledgeable about HPV and show generally positive attitudes and beliefs about HPV education and vaccination.

"Understanding head and neck surgeons' current knowledge, practice and opinions regarding human papillomavirus (HPV) education and prevention will enable efforts to assist surgeons in this important endeavor," authors wrote.

The study, published in the journal *JAMA Otolaryngology — Head & Neck Surgery*, used an online survey of members of the American Head and Neck Society (AHNS) and found more than 90 percent of respondents discuss risk factors for head and neck cancer and HPV as a specific risk factor with their patients. The authors also found that of those respondents with daughters, 68.9 percent reported that their daughters had received or they intend their daughters to receive the HPV vaccine.

Respondents reported divergent attitudes toward HPV vaccination safety and efficacy, the study noted, adding that respondents were "overwhelmingly supportive of possible future ANHS activities to educate clinicians, increase public awareness, educate patients and advocate for health policy related to HPV."

"These findings support AHNS developing a strategic plan and actions to improve knowledge and reduce HPV infection among the American public," authors concluded.

For more information, see the study published online Aug. 29, 2013, in the journal *JAMA Otolaryngology — Head & Neck Surgery*.

Esthetic Dental Treatment May Not Improve Happiness

Findings of a recent study, presented at the British Psychological Society's Division of Health Psychology annual conference, show that dentists need the support of health psychologists to enhance patients' satisfaction with their appearance before they embark on esthetic dental procedures.

The study, led by Sharmila Sarin and supervised by Koula Asimakopoulou, PhD, BSc, consisted of 60 participants who each completed the Slade Body Satisfaction Scale and a Visual Analogue Scale assessing satisfaction with their appearance before and after their dental work, according to a news release from the British Psychological Society. Study participants also completed a short version of the Big Five personality test before their operation.

Irrespective of the dental procedure performed, people who were happiest about their appearance before receiving esthetic dental work were those who were also the happiest after treatment; dissatisfaction with one's appearance seen in those high on neuroticism persisted after the esthetic dental work.

"We wanted to establish whether personality and the views that people have about their appearance before receiving esthetic dental treatment would influence satisfaction with the outcomes of esthetic dental procedures," said Sarin and Asimakopoulou. "We found that it is in the patients' and dentists' interest to ensure that patients receiving esthetic dental work start from as high a point of satisfaction with current appearance as possible. This will enhance the chances that they will be satisfied with the results of esthetic dental treatment. Neuroticism is also likely to interfere with satisfaction with esthetic dental work."

For more information, visit www.bps.org.uk/news/new-smile-may-not-make-you-happy.

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Kids' Healthy Mouths Campaign Shows Success In Survey

More parents report regularly monitoring and maintaining their child's oral health, therefore more children are regularly brushing, according to a survey administered by the Ad Council one year after the *Kids' Healthy Mouths* campaign began.

Launched in August 2012 by the Ad Council and the Partnership for Healthy Mouths, Healthy Lives, the campaign has received tremendous media exposure through widespread TV, radio, print, outdoor and digital public service announcements (PSAs) in both English and Spanish.

With a goal of reducing the prevalence of dental decay by motivating parents to promote good oral health habits with their kids, the campaign has, according to the recent survey, had the following impact:

- More than 50 percent of parents surveyed have seen or heard the new *Kids' Healthy Mouths* PSAs.
- Significantly more parents in 2013 report that their child brushes at least twice a day compared to before the campaign launched (55 percent of English-speaking parents in 2013, up from 48 percent in 2012, and 77 percent of Spanish-speaking parents in 2013, up from 69 percent in 2012).
- Parents in 2013 were also more likely to report their child brushes for at least two minutes each time (64 percent of English-speaking parents in 2013, up from 60 percent in 2012, and 77 percent of Spanish-speaking parents in 2013, up from 69 percent in 2012).
- An increased number of English- and Spanish-speaking parents report being "good" or "very good" at making sure their child brushes at least twice a day (65 percent of English-speaking parents in 2013, up from 60 percent in 2012, and 77 percent of Spanish-speaking parents in 2013, up from 73 percent in 2012) for two minutes each time (58 percent of English-speaking parents in 2013, up from 53 percent in 2012, and 79 percent of Spanish-speaking parents in 2013, up from 75 percent in 2012).

For more information, visit 2min2x.adcouncil.org.

UPCOMING MEETINGS

2013	
Nov. 3–9	U.S. Dental Tennis Association, Big Island, Hawaii, 800.445.2524 or dentaltennis.org
Nov. 10–13	National Primary Oral Health Conference, Denver, nnoha.org/conference/npohc.html
2014	
May 15–17	*CDA Presents The Art and Science of Dentistry*, Anaheim, 800.CDA.SMILE (232.7645) or cdapresents.com
Sept. 4–6	*CDA Presents The Art and Science of Dentistry*, San Francisco, 800.CDA.SMILE (232.7645) or cdapresents.com

To have an event included on this list of nonprofit association continuing education meetings, please email Courtney Grant at courtney.grant@cda.org.

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Dental Student Research

CHARLES J. GOODACRE, DDS, MSD, MS

One of the greatest satisfactions an educator can receive is to participate in the personal and professional growth of students. In fact, one of the greatest pleasures I have received is seeing students exceed the knowledge and skills of their teachers. After all, how can the continuum of dental progress be perpetuated without graduating students whose development progresses to the point where they exceed the accomplishments of their faculty?

GUEST EDITOR

Charles J. Goodacre, DDS, MSD, MS, is a diplomate of the American Board of Prosthodontics and a Fellow of the American College of Prosthodontists. He is a professor in the Department of Prosthodontics and former dean at Loma Linda University School of Dentistry.

Conflict of Interest Disclosure: None reported.

This issue is dedicated to highlighting student research and includes papers from four of the dental schools in California. Coupled with the guidance of their faculty, these students have created exceptional publications covering the basic and clinical sciences. The first article is about the use of cone beam computed tomography in the assessment of defect volume of cleft lip and palate patients. The second article is a study of serum markers for bisphosphonate-associated jaw osteonecrosis. The third article is a study that demonstrates how light activation of a photosensitizing agent can enhance cytotoxicity and be of beneficial use in the treatment of periodontal pathogens. The fourth article is about mediators of oral squamous cell carcinoma tumor invasion. These four excellent articles demonstrate the commitment of our students to expanding knowledge through research. In this issue, we salute our students, their faculty mentors and the importance of research to improved patient care. ■■■■

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Volumetric Assessment of Cleft Lip and Palate Defects Using Cone Beam Computed Tomography

DAVID LEE, BS; ELISA ATTI, MS; JAMES BLACKBURN, BS; SANDRA YEN, BS; DEBORAH LEE, BA; SOTIRIOS TETRADIS, DDS, PHD; AND CHRISTINE HONG, DMD, MS

ABSTRACT A possible avenue to improve the clinical success of bone graft procedures in cleft lip and palate cases is to predetermine the bone donor site and the volume of graft material required for the recipient site. This study utilized cone beam computed tomography to generate three-dimensional reconstructions and volumetrically assess unilateral cleft lip and palate defects. Access to this information can assist in determining an optimal donor site for secondary alveolar bone grafting.

AUTHORS

David Lee, BS, is a dental student at the University of California, Los Angeles, School of Dentistry.
Conflict of Interest Disclosure: None reported.

Elisa Atti, MS, is a research associate in Research Laboratory Support at the University of California, Los Angeles, School of Dentistry.
Conflict of Interest Disclosure: None reported.

James Blackburn, BS, is a dental student at the University of California, Los Angeles, School of Dentistry.
Conflict of Interest Disclosure: None reported.

Sandra Yen, BS, is a dental student at the University of California, Los Angeles, School of Dentistry.
Conflict of Interest Disclosure: None reported.

Deborah Lee, BA, is a research associate at the University of California, Los Angeles, School of Dentistry.
Conflict of Interest Disclosure: None reported.

Sotirios Tetradis, DDS, PhD, is a professor and the chair of the Section of Oral and Maxillofacial Radiology in the Division of Diagnostic and Surgical Sciences at the University of California, Los Angeles, School of Dentistry.
Conflict of Interest Disclosure: None reported.

Christine Hong, DMD, MS, is an assistant professor of the Section of Orthodontics in the Division of Associated Clinical Specialties at the University of California, Los Angeles, School of Dentistry.
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Cleft lip with or without cleft palate (CL/P) is the most common congenital deformity and affects approximately 8 per 10,000 live births each year in the United States.[1] CL/P patients suffer from a multitude of associated problems including eating difficulties, speech disorders, hearing impairments and social discomfort because of physical appearance. The treatment of CL/P patients requires a multidisciplinary approach with comprehensive and sequential procedures throughout the first two decades of life or more. A series of crucial steps in the treatment process involves maxillary expansion followed by cleft repair with a bone graft, termed "secondary alveolar bone graft."[2] Expansion is imperative in CL/P patients because they are typically

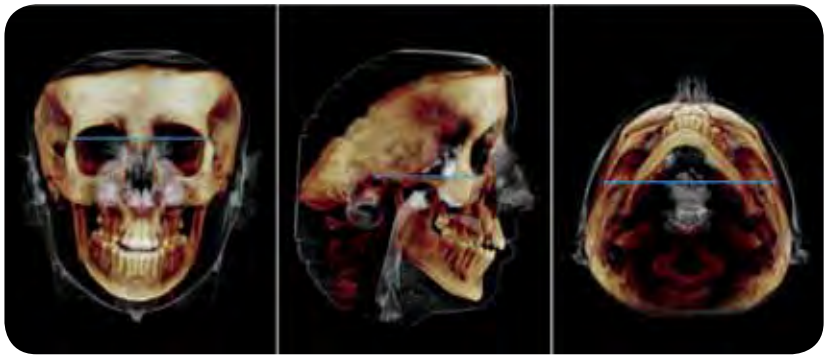

FIGURE 1. Orientation protocol on a CBCT image. Left: Align Z-points horizontally on lateral borders of the orbits from anterior view. Middle: Orient Frankfort plane horizontally on right porion and right orbitale on right lateral view. Right: Orient ZT-points horizontally on medial terminations of the zygomaticotemporal sutures on inferior view.

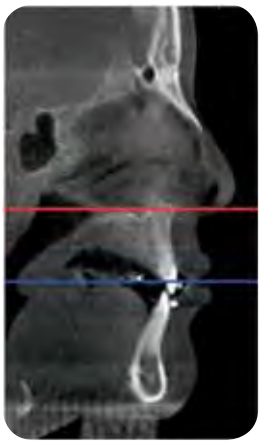

FIGURE 2. Superior and inferior boundaries of cleft. Superior boundary (red) at level of anterior nasal spine and inferior border (blue) at level of most inferior border of alveolar ridge identified on sagittal plane using DataViewer.

born with a narrow maxilla. Once sufficient width of the maxilla is achieved, the widened cleft is repaired through bone graft placement to close the oronasal fistulae, reconstruct the maxillary arch and guide the eruption of the cleft-adjacent permanent tooth, usually the canine, into the cleft area[3] to further stabilize and maintain newly formed bone.

Freshly harvested autogenous cancellous bone is ideal for alveolar cleft bone grafts because it supplies living, immunocompatible bony cells that integrate with the maxilla and are essential for osteogenesis.[4] Currently, the main donor site of autogenous bone is the iliac crest;[5] however, some authors report considerable morbidity associated with this donor site.[6-12] Complications encountered from iliac crest alveolar bone grafting include prolonged postoperative pain which limits walking, delayed healing, unsightly scaring and fracture of the iliac crest.[7] Other donor sites include the cranial bone,[13] mandibular symphysis[14] and tibia,[15] which have reports of decreased morbidity and fewer complications.[13-15] Optimal autograft donor site selection must take into account the volume of bone required for the graft as the cranial bone and the mandibular symphysis offer less bone volume than the iliac crest.[4]

Currently, the most frequently used imaging modality for presurgical planning is an orthopantogram along with an occlusal view;[16] however, accurate assessment of the cleft size and determination of bone volume required for the alveolar graft is difficult because of distortion, structural overlap, limited identifiable landmarks, and most importantly, no volumetric information.[17,18] In fact, because of the two-dimensional (2-D) nature of the current imaging modality, the number of clefts that can be successfully treated by bone grafts can be overestimated by 17 percent.[19] In other studies, authors have reported an under- or overestimation of bone support for cleft-adjacent teeth after primary bone graft by up to 25 percent using 2-D radiographs, as compared to CT scans.[20,21] These imaging deficiencies can lead to decreased prognostic accuracy resulting in overtreatment or failure to address clinically unsuccessful bone graft procedures.

The popularity of cone beam computed tomography (CBCT) as an imaging modality has been rising in the last decade. CBCT allows clinicians to perform better treatment planning because of its precise assessments of shape, quality (cortical and cancellous), height and thickness of the bone through multiplanar reconstructions.[22] CBCT permits the high-definition visualization of anatomic structures through sections made in the sagittal, axial or horizontal planes.[23] Other benefits of CBCT include a lower radiation dose, lower cost and smaller physical footprint as compared to other CT methods.[24-27] Most routine orthodontic patients do not require successive CBCT scans but in cases of craniofacial anomalies, CBCT has shown to improve planning of the treatment approach and evaluating treatment results.[28] Because of CBCT's superior accuracy, reproducibility and image quality, it was used in this study to replace traditional radiographs.

The purpose of this study is to validate CBCT as a method to quantitatively measure the volume of alveolar deficits in patients with nonsyndromic unilateral cleft lip and palate. Volume of cleft sites was calculated and a 3-D reconstruction was generated with SkyScan software (Bruker-microCT, Kontich, Belgium). Access to this information prior to secondary alveolar bone grafting can aid in determining an optimal donor site for grafting into alveolar deficits.

Methods

A prospective clinical cohort study was performed. Study protocol was approved by the UCLA Medical Institutional Review Board (IRB #04-11-014-01), the UCLA Radiation Safety Division and the Medical Radiation Safety Committee. Informed consent was obtained. Seven subjects from the UCLA graduate Orthodontic Clinic and Craniofacial Clinic were included in this study. Selected subjects had nonsyndromic, complete unilateral cleft lip and palate and had plans to undergo bone graft surgery. All patients underwent maxillary palatal expansion prior to bone graft surgery.

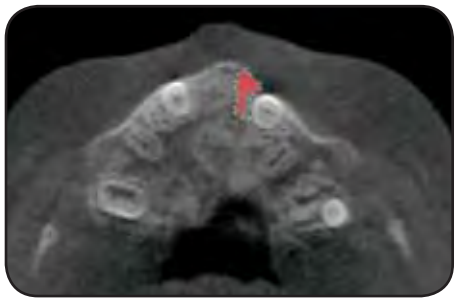

FIGURE 3. Manual outline of cleft site. Boundaries of cleft were outlined on an average of 46 axial slices using the "regions of interest" feature in CTAn. Shape of cleft is shown in red.

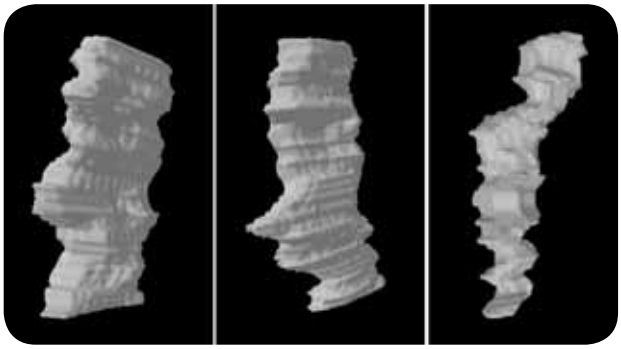

FIGURE 4. 3-D reconstruction of cleft site is generated from axial slices that contained manual outlines of cleft using CTVol.

Exclusion criteria included bilateral cleft lip and palate, craniofacial syndromes, maxillofacial pathosis (excluding caries or gingivitis), history of trauma to maxilla or mandible, history of previous oral maxillofacial surgery or orthognathic surgery or refused study enrollment.

The first CBCT scan was taken after orthodontic expansion and immediately before surgery (T1), and the second scan was taken within one month of graft placement (T2). To ensure accuracy, all measurements were performed by two raters. At T1, the volume of the cleft (V_c) was computed; at T2, the volume of the bone graft (V_b) was computed. CBCT scans were captured using the NewTom 3G (AFP Imaging, Elmsford, N.Y.). Scans with the NewTom 3G were performed using a 12-inch field of view, 12-bit gray scale and a 0.4 mm isotropic voxel. The scans were converted into DICOM-3 format and then exported to Dolphin Imaging (Version 11.0.3.9, Dolphin Imaging, Chatsworth, Calif.). To standardize head orientation, a method of 3-D orientation was developed. The Z-Points, Frankfort Plane and ZT-Points were all oriented horizontally (**FIGURE 1**). Position of the subject within the 3-D matrix was standardized by recalculation of Cartesian coordinates after each volume was oriented.

Dicom files were then converted into bit map (BMP) format using XnView (XnSoft, Reims, France) software. BMP files were then analyzed by DataViewer, CTAn and CTVol, which are features of the volume-rendering software SkyScan.

Using DataViewer, the superior and inferior boundaries of the cleft were identified on a sagittal plane. The anterior nasal spine was identified as the superior border, while the most inferior border of the alveolar ridge was identified as the inferior border (**FIGURE 2**). Using CTAn, areas of the cleft site were manually outlined on an average of 46 axial slices (**FIGURE 3**) using the "regions of interest" feature, and a 3-D reconstruction of the cleft site was generated using CTVol (**FIGURE 4**). The volume of the cleft was then calculated via the "3-D analysis results."

To ensure accuracy, all measurements were performed by two measurers. Statistical analyses were performed on the data using Stata (Release 12, StataCorp LP, College Station, Texas). The mean, standard deviation, standard error and 95 percent confidence intervals were computed. A Pearson's coefficient of correlation was used to measure the relationship between V_c and V_b. Inter-rater reliability was computed.

Results

Seven unilateral complete cleft lip and palate patients were ages 8.8 to 14.8 years (mean age = 11.4 years, SD = ± 2.0) (**FIGURE 5**) upon initial examination. There were four females and three males. The ethnic makeup of the subjects was three of Hispanic descent, two of Caucasian descent, one of Japanese descent and one of Filipino descent.

The volume of the clefts was largely variable, ranging from 1.2 to 5.1 cm^3. In six of the seven subjects, V_b was higher than V_c. The mean V_c at T1 was 2.4 ± 1.2 cm^3 (range, 1.2 to 4.7 cm^3; 95 percent CI, 1.7-3.1 cm3). At T2, the mean V_c was 2.5 ± 1.3 cm^3 (range, 1.2 to 5.1 cm3, 95 percent CI, 1.7-3.2 cm^3) (**FIGURE 6**). The mean V_b was slightly greater than the mean V_c by 0.15 cm3. V_c and V_b had a Pearson correlation coefficient of r = 0.96, indicating a strong positive correlation.

Inter-rater reliability was measured by an Intraclass correlation coefficient (ICC) using a two-way, random-effects model specifying absolute agreement. An ICC value of > 0.90 was achieved, indicating an excellent agreement between repeated measurements on an individual subject.

Discussion

CL/P results in several clinically significant deficiencies including dental crossbite,[29,30] facial deformities,[31] nasal airway impairments[32] and the ectopic eruption of teeth.[33] A critical step in the treatment of CL/P is the bone graft placement in the cleft to permit the proper eruption of teeth,[34] obtain maxillary arch continuity, maximize bone support for dentition and establish alveolar morphology.[35] Clinicians treating CL/P patients have long struggled with the high failure rate of secondary alveolar bone graft, leading to repeated surgeries. With several potential donor sites, each associated with varying levels of morbidity and a limited volume of available bone, CBCT

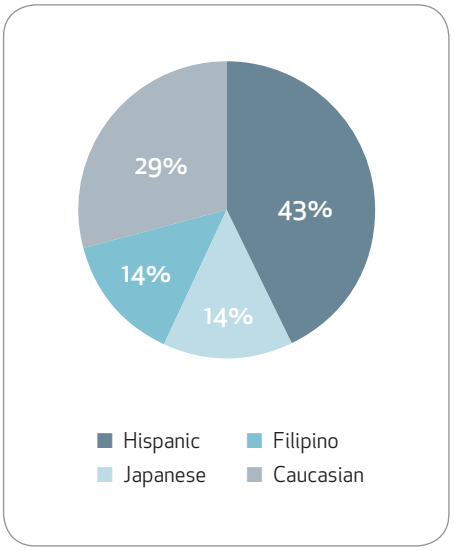

FIGURE 5. Ethnicities of study subjects. Ethnic makeup of subjects was three Hispanic, two Caucasian, one Japanese and one Filipino.

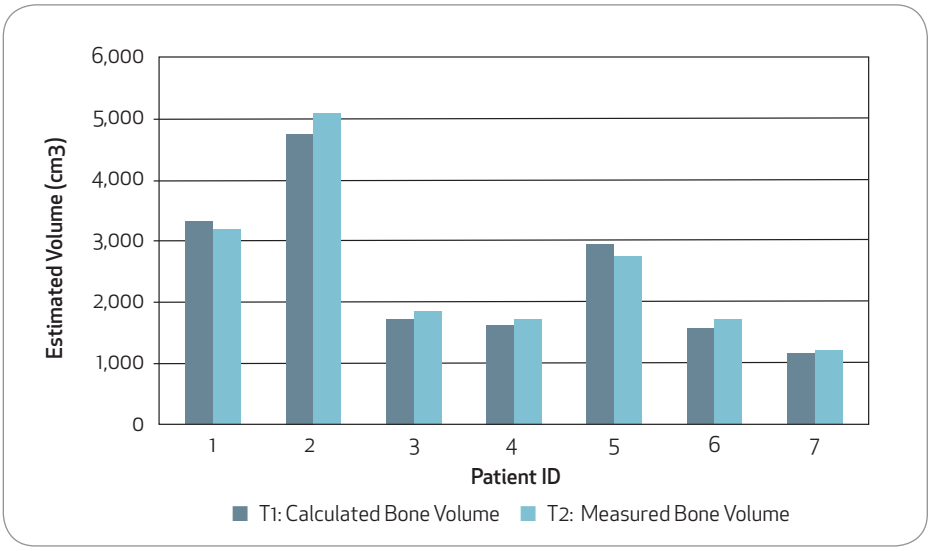

FIGURE 6. Graft volumes at T1 and T2. Calculated bone volume at T1 (dark blue) and measured bone volume at T2 (light blue) for patients.

can increase chances of clinical success by allowing both the surgeon and the patient to predetermine the donor site that will have the lowest level of morbidity while simultaneously ensuring that an adequate volume of bone is available for grafting.

Traditional 2-D radiographs do not depict depth or bone volume in cleft sites needing alveolar bone graft and overestimate the amount of bone grafts needed for clinical success. Magnetic resonance imaging (MRI) has high cost, requires a horizontal scanning position of the patient, and most importantly, does not offer an acceptable level of skeletal definition.[36] Shortcomings of other imaging modalities include distortion of the surface texture (3-D ultrasonography), sensitivity to light and metal objects (3-D laser surface scanning) and increased radiation dosage (multislice CT), which make them less than ideal for CLP patients.[36]

While CBCT imaging has been criticized for its higher radiation dose as compared to traditional 2-D imaging techniques (lateral cephalogram, panoramic and a complete-mouth radiographic series), studies show that CBCT radiation exposure is relatively low when compared to other modalities. CBCT radiation exposure ranges from 20µSv-599µSv for a full craniofacial scan,[37] while the cumulative radiation exposure of the traditional 2-D imaging techniques is 47µSv-420µSv.[38] The NewTom 3G machine that was used for the CBCT images of the patients in this study yields an effective radiation dose of 68µSv. For comparison purposes, a conventional spiral CT of the head produces an effective radiation dose of 2,000µSv. With its increased amount of diagnostic information and relatively lower radiation dose, CBCT scans may be an appropriate imaging modality for studies that involve cleft lip and palate patients.[24]

Studies on the utilization of CBCT to volumetrically assess alveolar cleft defects are limited. Quereshy et al.[16] estimated the volume of the cleft using three measurements: facial width, facial height and facial-palatal length prior to secondary repair of the alveolar cleft. In this study, the volumetric reconstruction was based on manually identifying the outline of the cleft on an average of 46 axial slices, increasing accuracy of volumetric measurement. Oberoi et al.[39] took CBCT scans before grafting, as well as at least one year after graft placement to measure the residual defect under the assumption that grafted bone would be difficult to distinguish from adjacent alveolar bone. The raters experienced minimal difficulty differentiating new bone from existing bone on the CBCT scans, and favored a one-month follow-up period to Oberoi et al.'s one-year follow-up due to the possibility of bone resorption. Bone resorption would lead to a less accurate V_b measurement, as documented in previous studies.[40-43] For example, Zhang et al. found an average bone loss of 36 percent after three months and 56 percent after six months in alveolar bone grafts.[42]

While our protocol did not include the measurement of actual bone volume used in the bone grafting operation, our average computed volume closely mirrors the average bone volume used in standard secondary alveolar bone grafting procedures,[44] as well as procedures that used CT imaging.[45,46] The results of our study suggest that CBCT could be a valuable aid in treatment planning in patients with CLP, as it is a reproducible and reliable method of volumetric evaluation of the cleft site to estimate defect volume. The large variability evident in the cleft sites of the cohort further supports the need for accurate predetermination of cleft volume.

Conclusion

We validated CBCT imaging and analysis as a reproducible method of 3-D evaluation of the unilateral cleft lip and palate with SkyScan software that can be used to estimate the volume of the defect. While our results are encouraging, more experiments must be completed before CBCT becomes the main imaging modality in the treatment of patients with CLP. ■■■■

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THE CORRESPONDING AUTHOR, Christine Hong, DMD, MS, can be reached at chong@dentistry.ucla.edu.

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Evaluation of Serum Biomarkers IL-17 and CTX for BRONJ: A Pilot Clinical Case-control Study

PETER B. LEE, DDS; ANDREW S. KISS, DDS; ANDREW L. NGUYEN, BS; SONGTAO SHI, DDS, PHD; PARISH P. SEDGHIZADEH, DDS, MS; AND ANH D. LE, DDS, PHD

ABSTRACT A serious complication of bisphosphonate (BP) therapy is BP-related osteonecrosis of the jaw (BRONJ). Currently, no biomarkers exist to identify patients at risk. We evaluated whether interleukin-17 and C-telopeptide correlate with BRONJ development. We conducted a case-control study using patients with a history of BP therapy. Quantitative enzyme-linked immunosorbent assay and Student's t-test were done. Both markers were significantly higher in BRONJ, suggesting altered immune responses and bone remodeling may play roles in BRONJ development.

AUTHORS

Peter B. Lee, DDS, is a 2013 graduate of the Herman Ostrow School of Dentistry of the University of Southern California. *Conflict of Interest Disclosure: None reported.*

Andrew S. Kiss, DDS, is a 2013 graduate of the Herman Ostrow School of Dentistry of the University of Southern California. *Conflict of Interest Disclosure: None reported.*

Andrew L. Nguyen, BS, is a 2015 DDS candidate at the Herman Ostrow School of Dentistry of the University of Southern California. *Conflict of Interest Disclosure: None reported.*

Songtao Shi, DDS, PhD, is a professor at the Herman Ostrow School of Dentistry of the University of Southern California, Center for Craniofacial Molecular Biology. *Conflict of Interest Disclosure: None reported.*

Parish P. Sedghizadeh, DDS, MS, is director of the University of Southern California Center for Biofilms and an assistant professor of Clinical Dentistry. *Conflict of Interest Disclosure: None reported.*

Anh D. Le, DDS, PhD, is chair and Norman Vine endowed professor in the Department of Oral and Maxillofacial Surgery and Pharmacology at University of Pennsylvania in Philadelphia. She was professor, Career Academic, Division of Endodontics, Oral and Maxillofacial Surgery and Orthodontics, at the Herman Ostrow School of Dentistry of the University of Southern California, and the Center for Craniofacial Molecular Biology. *Conflict of Interest Disclosure: None reported.*

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Bisphosphonate (BP) medications are the most commonly prescribed class of antiresorptive drugs, used to treat bone disorders such as osteoporosis and cancer-associated skeletal complications.[1] A serious adverse effect of BP therapy is BP-related osteonecrosis of the jaw (BRONJ), characterized by necrotic jaw bone in the oral cavity.[2] The pathogenesis of BRONJ remains uncertain, and is currently hypothesized to be multifactorial, usually involving oral surgery or trauma with subsequent delayed wound healing, altered jaw bone remodeling and a biofilm-mediated infection.[3,4,5]

Risk factors for BRONJ include invasive dental procedures or oral trauma, infection, increasing age, ethnicity,

length of exposure to BP, co-morbidities, cancer and concomitant use of immunosuppressives and chemotherapeutics.[6,7,8] Because many cancer patients are on multiple immunosuppressant drugs, including steroids and chemotherapeutic agents, it is possible that altered immune responses contribute to an increased risk for BRONJ. Currently, no clinical biomarkers exist to identify patients at risk for BRONJ. Recent human and animal studies suggest that serum immune markers, such as specific subsets of T-cells (e.g., T_h-17 and γδ–T) may serve as predictors for risk of BRONJ.[9,10] Some investigators also suggest that certain serum bone turnover markers (e.g., C-telopeptide or CTX) can predict risk for BRONJ or guide therapeutics,[11] although this is currently controversial and disputed by other investigators.[12] Overall, an urgent need exists for the discovery of candidate biomarkers for BRONJ with the potential to aid in prevention or inform intervention.

Therefore, in this pilot clinical case-control study we evaluated whether the serum marker interleukin-17 (IL-17), an immune cytokine produced by T_h-17 cells, and the serum bone turnover marker CTX, correlate with BRONJ.

Materials and Methods

This human subject research was carried out in accordance with the International Ethical Guidelines and Declaration of Helsinki and approved by the University of Southern California Institutional Review Board (IRB). Patients were screened and recruited from the Oral Medicine Clinic at the Ostrow School of Dentistry and the BRONJ clinic in the Outpatient Dental Clinic at the LAC+USC Medical Center. All patients were administered a standardized health history and medical record covering history of cancer, chemotherapy, BP use and dental history, and received a complete head and neck and oral examination and radiographic examination when applicable.

Patients with BRONJ were identified and diagnosed based on standard clinical and radiographic protocols of the American Association of Oral and Maxillofacial Surgeons (AAOMS) BRONJ case definition:[13] 1) current or previous treatment with BP; 2) exposed, necrotic bone in the maxillofacial region that has persisted for more than eight weeks and 3) no history of radiation therapy to the jaw. For case subjects (BRONJ), the inclusion criteria were: 1) all patients who have been treated with chemotherapy and intravenous (IV) BP for >1 year; 2) patients treated with oral BP for osteoporosis or prevention of osteoporosis for >1 year; 3) clinical diagnosis of BRONJ at any stage as established by standard clinical and radiographic protocol per AAOMS diagnostic criteria;[13] 4) willingness to have photographs taken to document lesions and 5) willingness to consent to venipuncture for serum sample collection. For control subjects without BRONJ (non-BRONJ), the inclusion criteria were: 1) patients without BRONJ who had been treated with chemotherapy and IV BP for >1 year; 2) Patients treated with oral BP for osteoporosis or prevention of osteoporosis for >1 year; 3) no clinical signs or symptoms of BRONJ; 4) willingness to consent to venipuncture for serum sample collection. To minimize confounder or effect modifiers, the following exclusion criteria were applied to all patients: 1) history of radiation therapy to the head and neck to exclude osteoradionecrosis patients; 2) active systemic infection, diabetes or rheumatoid arthritis which could alter serum immune profiles; 3) patients with cognitive, language or hearing problems were not recruited to ensure that every patient could provide his/her own consent. All cases and controls were selected by a board-certified oral and maxillofacial surgeon (ADL) and a board-certified oral and maxillofacial pathologist (PPS) independently.

For specimen acquisition, phlebotomy was performed and two vials (10 ml) of blood were acquired from each patient in the BRONJ group and non-BRONJ control group. The blood samples were processed by quantitative enzyme-linked immunosorbent assay (ELISA) for IL-17 and CTX evaluation using our standardized laboratory protocols as previously described,[10] with

TABLE

Summary of Study Population Parameters

Characteristic	BRONJ (n=9)	Non-BRONJ (n=9)
Age range	65-85	60-85
Sex		
Male	3	4
Female	6	5
Ethnicity		
African American	0	1
Asian	3	4
Caucasian	3	2
Hispanic	3	2
Initial disease stage		
0	0	n/a
1	2	n/a
2	7	n/a
3	0	n/a
Co-morbidities		
Cancer history	5	2
Osteoporosis	4	7
BP route of administration		
Oral	4	7
IV	5	2

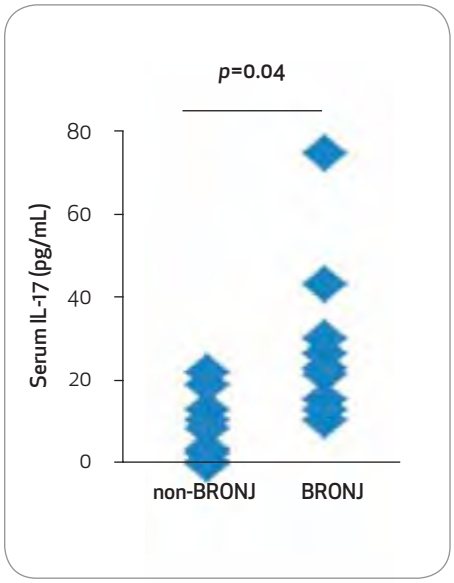

FIGURE 1. Elevated expression of IL-17 in serum of BRONJ patients. Serum samples were collected from control patients with a history of BP treatment without clinical BRONJ (non-BRONJ), and cases manifesting BRONJ lesions (BRONJ). IL-17 levels in serum were determined by ELISA and there was a statistically significant difference between cases and controls ($p<0.05$).

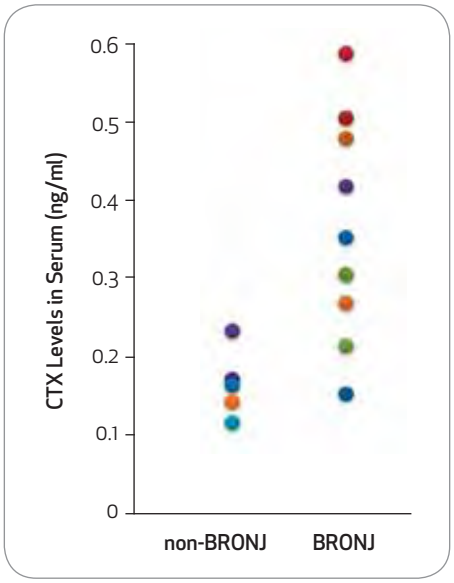

FIGURE 2. CTX levels in serum measured in ng/ml of non-BRONJ and BRONJ patients. The distribution for the BRONJ group is non-uniform as the CTX levels range from 0.15 to 0.6. The mean of CTX levels for the BRONJ group was 0.362 while for the non-BRONJ group was 0.165. The BRONJ group was significantly associated with a higher mean value of CTX than the non-BRONJ group ($p=0.000612$).

triplicate measurements performed to ensure reproducibility of results. Our rationale for focusing on and selecting these specific serum markers for evaluation was not random or arbitrary; but rather predicated on: 1) known or assumed associations with BRONJ pathophysiology; 2) mechanistic plausibility and 3) previous human and animal studies and data into BRONJ. For comparison of IL-17 and CTX values between cases versus controls, statistical analysis was performed using the Student's *t*-test (Systat Software Inc., Point Richmond, Calif.), and *p* values <0.05 were considered significant.

Results

Study Population

The clinicopathologic and demographic characteristics of the study population are summarized in the **TABLE**. There were 18 patients comprising BRONJ cases (n=9) and non-BRONJ controls (n=9) for final analysis after applying all aforementioned ascertainment criteria. In the BRONJ group, six patients were female and three male. In the non-BRONJ control group, five patients were female and four male. The mean age of the BRONJ group was greater than the control group. Seven cases in the BRONJ group represented stage 2 disease and two cases represented stage 1 disease. Five BRONJ cases had a history of cancer including multiple myeloma (n=3), breast (n=1) and prostate (n=1) cancer, and four cases had a history of osteoporosis. All cancer patients had a history of IV zoledronate use as compared to osteoporosis patients who were on some form of oral BP (alendronate, risedronate, ibandronate). In the non-BRONJ control group, two patients were diagnosed with cancer and were receiving IV BP therapy. Seven patients were treated with oral BP (alendronate, risedronate, ibandronate) for osteoporosis.

Serum Markers

Both serum markers evaluated in this study were significantly increased in BRONJ cases versus non-BRONJ controls. **FIGURE 1** shows serum IL-17 expression was significantly higher in BRONJ cases versus controls ($P=0.04$). The mean serum IL-17 level was 28.90±19.94 pg/ml in BRONJ group versus 9.07±8.12 in non-BRONJ controls.

FIGURE 2 shows serum CTX levels were significantly higher in BRONJ cases versus controls ($P=0.000612$). For CTX measurements, only five control cases provided reproducible and accurate results sufficient for analysis. The mean serum CTX was 0.36 ± 0.14 ng/ml in BRONJ cases versus 0.16±0.05 ng/ml in non-BRONJ controls. Unlike previously reported,[11] the serum CTX values are consistently higher in both control and BRONJ cases, which may reflect the random blood sampling in our study.

Discussion

In an effort to explore potential biomarkers for BRONJ, our group recently developed an experimental model of BRONJ-like disease in mice[10] and swine[14] using IV zoledronate, a potent BP. Our animal models revealed that an underlying altered immune mechanism, specifically the activation of inflammatory T-helper producing IL-17 cells (T_h-17) and suppression of regulatory T-cells (T-regs) in peripheral blood, was associated with a high incidence of BRONJ. The purpose of the current study was to clinically test and validate previous findings in our animal models. We further sought to evaluate whether bone turnover markers, such as CTX show any correlation with BRONJ as previously suggested.[11]
In daily activities, jawbones are cyclically strained, such as during chewing, which can lead to microdamage and alterations in bone remodeling.[15] BP therapy can further

affect jawbone remodeling. The CTX bone turnover marker is a straightforward tool to assess the bone turnover/renewal suppression caused by BP, and has been proposed as an indicator of BRONJ risk.[11] Currently, there is no consistent data supporting the use of a CTX marker to predict development or treatment response in BRONJ patients.[16,17] Here, we explored another mechanistically plausible biomarker in conjunction with CTX to evaluate BRONJ risk in our pilot case-control study.

Recent studies provide direct evidence that BP therapy can affect the innate immune system, including inhibition of neutrophil enzymes that affect wound healing,[18] increased risk of neutropenia and decreased generation of reactive oxygen species.[19] This is not surprising in view of the mechanism of action of BP drugs, which target small GTPases that are signaling proteins integral to neutrophil differentiation and function.[20]

The negative effects of BP drugs on the immune system are also amplified by several comorbidities commonly seen in the segment of the population receiving BP therapy. For example, in cancer patients, which is the most common population affected by BRONJ, chemotherapeutic regimens can cause depression of the immune system by paralyzing the bone marrow and leading to leukopenia, erythropenia and thrombocytopenia.[21] Patients with autoimmune diseases such as rheumatoid arthritis, for example, rely heavily on corticosteroid therapy to induce remission or reduce disease severity.[22] Long-term treatment with corticosteroids may induce a transient lymphocytopenia by altering lymphocyte recirculation or inducing lymphocyte death. The most important immunosuppressive effect of corticosteroids is on T-cell function and adaptive immunity. Patients with diabetes mellitus, for example, suffer from increased infections because of an immunosuppressive state caused by altered immunity; the functions of neutrophils such as phagocytosis, chemotaxis and cytokine-production are decreased.[23] All of these factors and conditions contribute to altered immune responses, and coupled with BP use, are thought to increase the risk for developing BRONJ.

In summary, emerging evidence suggests that patients taking BP drugs can experience alterations of jawbone remodeling and alterations in both the innate and acquired immune pathways, possibly contributing to increased risk for BRONJ. Our preliminary findings suggest that serum markers IL-17, a cytokine produced by specific subsets of T-cells (e.g., T_h-17 and γδ-T), and CTX may be useful candidate markers to evaluate clinically for BRONJ risk. These results should be interpreted with caution and in consideration of several study limitations. First, the nature of the current preliminary study and the fact that the study is not prospective in nature means it does not represent a sufficiently high level of evidence for biomarker discovery, limiting any direct translation to clinical use or application. Second, the small number of patients and subgroups in this pilot study limits the generalizability of our results. Third, the markers selected for statistical analysis, and the type of analysis used, in lieu of other covariates, confounders or effect modifiers and analyses utilizing univariate or multivariate models also limits our findings. However, our findings suggest that this line of investigation at a higher level of evidence (e.g., well-controlled prospective cohort study), with larger patient populations and univariate and multivariate modeling may be warranted, and may provide useful insights into potential biomarkers for BRONJ development. ■■■■

THE MOST IMPORTANT immunosuppressive effect of corticosteroids is on T-cell function and adaptive immunity.

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THE CORRESPONDING AUTHOR, Peter B. Lee, DDS, can be reached at peterbclee@gmail.com.

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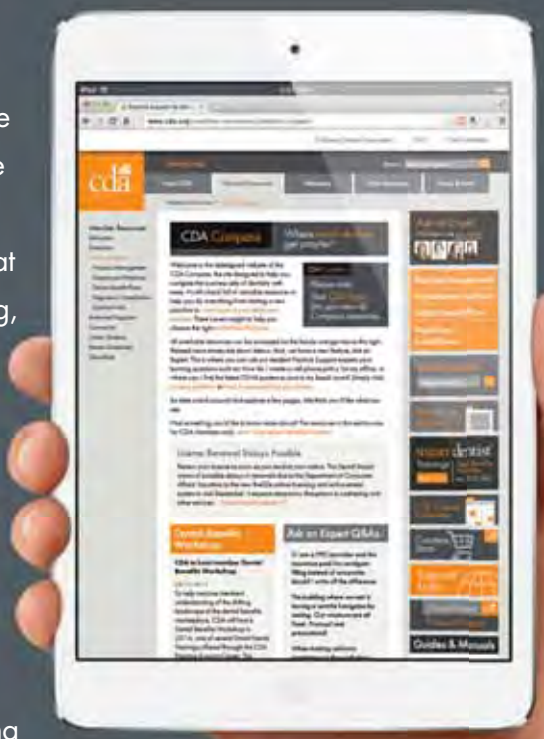

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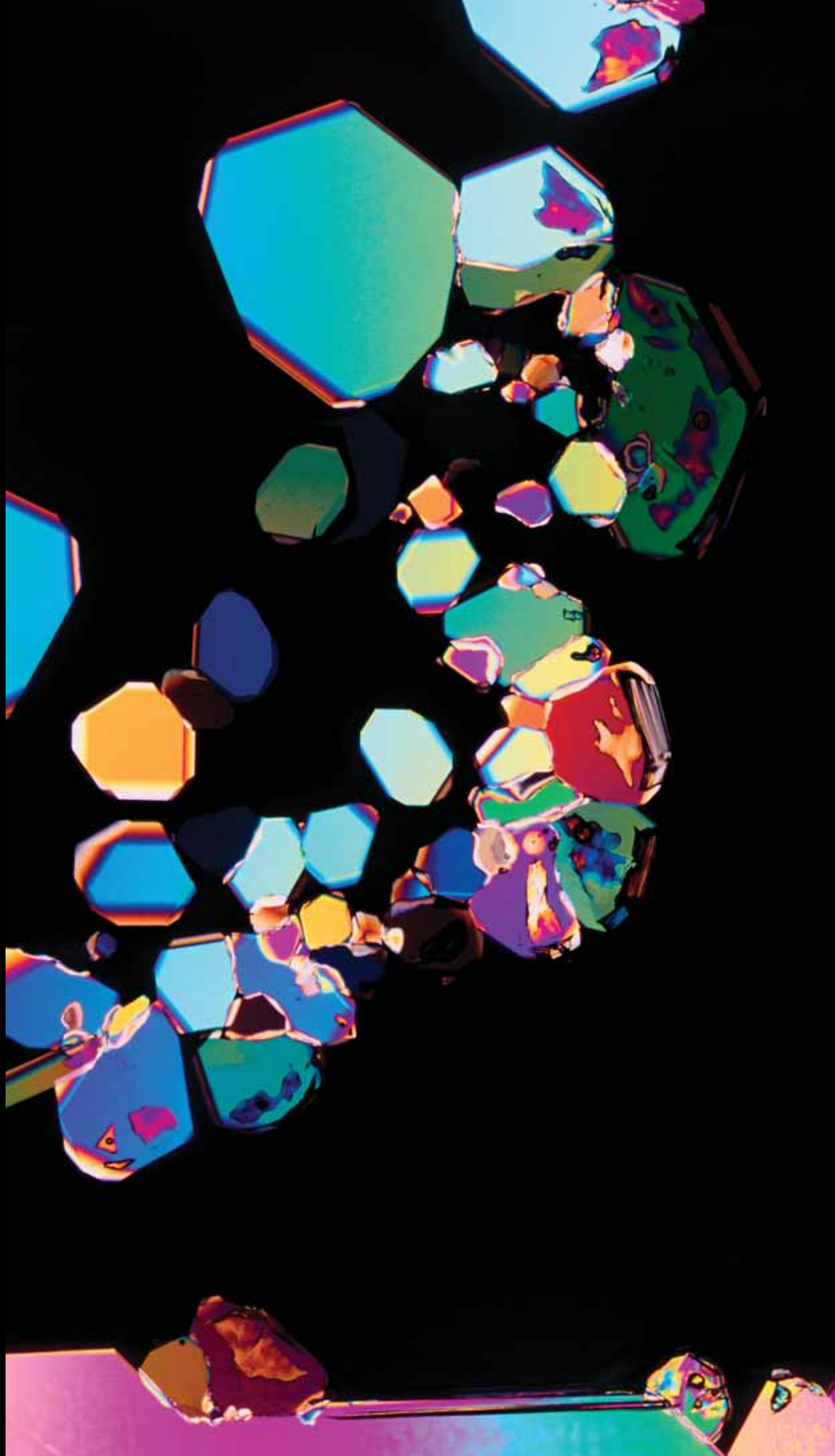

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Photodynamic Therapy of *Porphyromonas gingivalis* via Liposome-encapsulated Photosensitizers

ALEX KO; MICHAEL YEE; PAULINA SKUPIN-MRUGALSKA; AND NEJAT DÜZGÜNES, PHD

ABSTRACT Photodynamic therapy exploits the light-activation of a photosensitizer to cause cytotoxicity. Liposomes can be used to deliver hydrophobic photosensitizers to bacteria. Positively charged dioleoyltrimethylammoniumpropane:palmitoyloleoylphosphatidylcholine (1:1) liposomes bound quantitatively to the periodontal pathogen, *Porphyromonas gingivalis*. Following illumination, free and liposomal zinc phthalocyanine reduced the colony-forming unit (CFU) to 65 percent and 23 percent of controls, respectively. Thus, localization of the photosensitizer at the surface of bacteria via liposome binding enhanced the photodynamic cytotoxicity of zinc phthalocyanine.

AUTHORS

Alex Ko is a senior dental student at the University of the Pacific, Arthur A. Dugoni School of Dentistry in San Francisco. *Conflict of Interest Disclosure: None reported.*

Michael Yee is a research associate at the Microbiology Research Laboratory at the University of the Pacific, Arthur A. Dugoni School of Dentistry in San Francisco. *Conflict of Interest Disclosure: None reported.*

Paulina Skupin-Mrugalska is a PhD student at Poznan University of Medical Sciences in Poznan, Poland. She was a visiting scientist at the University of the Pacific, Arthur A. Dugoni School of Dentistry. *Conflict of Interest Disclosure: None reported.*

Nejat Düzgünes, PhD, is a professor and chair of the Department of Microbiology at the University of the Pacific, Arthur A. Dugoni School of Dentistry in San Francisco. *Conflict of Interest Disclosure: None reported.*

Gingivitis and periodontitis are some of the most prevalent infectious diseases in humans.[1] Periodontitis is an inflammatory disease characterized by progressive destruction of the periodontal ligament and alveolar bone. The most common form of periodontitis is chronic periodontitis. The potential pathogens in chronic periodontitis are usually Gram-negative anaerobic bacteria, including *Porphyromonas gingivalis*, Tannerella forsythia, Treponema denticola and Prevotella intermedia.[1] The proportion of Gram-negative anaerobic bacteria increases in human subgingival plaque samples as the severity of periodontal disease increases.[2] The increase in *P. gingivalis* in periodontal lesions has been correlated with the severity of periodontitis,[3] and the *P. gingivalis* virulence factors associated with tissue destruction have been identified.[4,5]

Although scaling and root planing is the first course of action in the treatment of periodontal disease, the use of systemic antibiotics such as azithromycin has significant clinical and microbiological benefits.[6,7] The adjunctive use of systemic antibacterial agents commonly used to treat oral bacterial infection is difficult to maintain at therapeutic concentrations in the oral cavity, and can be rendered ineffective by the development of drug resistance in the target organisms.

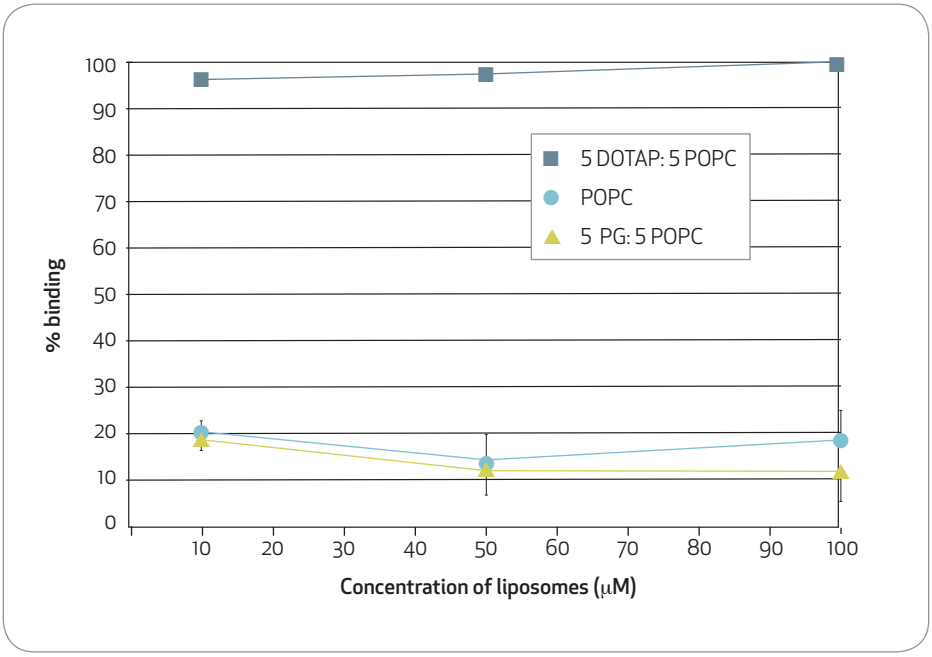

FIGURE 1. Liposome binding to *Porphyromonas gingivalis*. The percentage of fluorescently labeled liposomes incubated with *Porphyromonas gingivalis* that bound to the bacteria after a 30-min incubation. The data are given as the mean and standard deviation.

Photodynamic therapy (PDT) involves the use of a photosensitizer molecule and visible light to inactivate cells, and has been used for the treatment of some malignancies. Similar to PDT, photodynamic antimicrobial chemotherapy (PACT) is based on the concept that a nontoxic photosensitizer that accumulates in pathogens is subsequently activated by visible light of the appropriate wavelength to generate reactive oxygen species that are cytotoxic to the pathogen.[8] The reactive oxygen species can damage proteins, lipids and nucleic acids as well as other cellular components. The use of a photosensitizer and light as an antimicrobial treatment of periodontal microbial biofilms represents an attractive method for eliminating oral pathogenic bacteria.[8]

One critical issue for successful antimicrobial photodynamic therapy is the selective and sufficient binding of the photosensitizer to bacteria. Liposomes are lipidic nanoparticles that can incorporate hydrophobic photosensitizers in their membranes. Numerous liposomal photosensitizer formulations are in preclinical and clinical development, and the liposomal formulation of benzoporphyrin derivative monoacid (BPD; verteporfin), called Visudyne, has been approved for the treatment of macular degeneration.[9]

We investigated the ability of liposomes with different charge to bind *P. gingivalis*, using a fluorescent lipid incorporated in the liposome membrane. We also examined the effect of the photosensitizer, zinc phthalocyanine, free or encapsulated in liposomes, on the viability of *P. gingivalis*. Zinc phthalocyanine has low dark-toxicity, photochemical stability and strong absorption in the red region that can facilitate light penetration into tissues. Garcia et al.[10] have shown that encapsulation of zinc phthalocyanine in various liposomes prevents the dimerization or oligomerization of the photosensitizer, thereby conferring photodynamic activity to the molecule.

Materials and Methods

Bacterial Strain and Growth Conditions

P. gingivalis strain 2561 (ATCC 33277) was subcultivated on blood agar plates (Anaerobe Systems, Morgan Hill, Calif.), under anaerobic conditions, scraped gently from the agar and suspended in Medium 199 (Difco/Becton Dickinson, Franklin Lakes, N.J.) to an optical density of 0.1 at 660 nm (Nanodrop, Wilmington, Del.). This optical density is equivalent to 100 million bacteria/ml.

Liposomes

Liposomes were prepared by hydration of dry lipid films in isotonic buffer, followed by extrusion through polycarbonate membranes. Liposomes were composed of palmitoyloleoylphosphatidylcholine (POPC): phosphatidylglycerol (PG) (1:1), pure POPC or dioleoyltrimethylammoniumpropane (DOTAP):POPC (1:1), and also included 1 mole% of the fluorescent probe rhodamine-phosphatidylethanolamine (Avanti Polar Lipids, Alabaster, Ala.). The lipids were dissolved in chloroform (Fisher Scientific, Fremont, Calif.) and the solvent was evaporated to dryness in a rotatory evaporator (Labconco, Kansas City, Mo.) to deposit a lipid film on the walls of a test tube. To remove final traces of the solvent, the films were kept in a vacuum desiccator (Thermo Scientific Napco, Fremont, Calif.) for 12 h. Multilamellar vesicles were prepared by hydration of the dried lipid films under an argon atmosphere (achieved by flushing argon over the buffer) at a concentration of 10 μmol lipid/ml of 140 mM NaCl and 10 mM HEPES buffer (Sigma, St. Louis, Mo.) (pH 7.4), followed by vortexing for 10

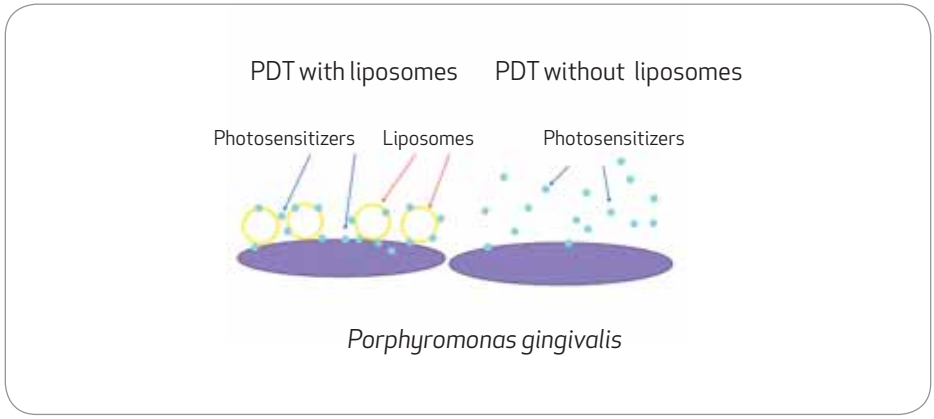

FIGURE 2. Schematic illustration of the interaction of free and liposome-encapsulated photosensitizers with *Porphyromonas gingivalis*.

min. Liposomes were extruded 21 times through polycarbonate membranes of 100-nm pore diameter, using the Avanti Mini-Extruder, to achieve a uniform size distribution. Liposomes were stored at 4° C under an argon atmosphere.

Liposomes used for photodynamic therapy were composed of DOTAP:POPC (1:1), and contained 1 mol% (i.e., 0.1 µmol in 10 µmol lipid) zinc phthalocyanine (Sigma), and no rhodamine-phosphatidylethanolamine.

Liposome Binding to P. gingivalis

Positively, neutrally or negatively charged liposomes were first pre-centrifuged at 14,000 rpm for 10 min in an Eppendorf 5418 centrifuge (Hamburg, Germany). This step was introduced to prevent the nonspecific pelleting of any large liposomes during the experiments on liposome binding to bacteria. The liposomes, in the concentration range 10-100 µM lipid, were incubated with 108/ml *P. gingivalis* in suspension for 30 min at room temperature. The bacteria were centrifuged at 14,000 rpm for 10 min in the Eppendorf centrifuge. Fluorescence levels of rhodamine in the supernatant and pellets were measured using a Perkin-Elmer LS-50B Luminescence Spectrometer (Waltham, Mass.).

Photodynamic Therapy

P. gingivalis cells were incubated with free or liposome-encapsulated zinc phthalocyanine for 2 h at 37° C in 96-well plates (BD Falcon, BD, Franklin Lakes, N.J.). Control, untreated *P. gingivalis* cells were incubated only with Medium 199. The plates were exposed to red light for 20 min at room temperature, using a DuraMax light bulb (75W, Med 120V A19 Cl/LL 20W; Philips Electronics North America Corporation, Andover, Mass.) with a red filter, at a distance of 10 cm from the light bulb to the plate. The radiation intensity at the level of the cells was 36 mW/cm2. Infrared radiation was minimized using a 1 cm water filter between the cell plates and the light source. Bacteria treated with the photosensitizer, but shielded from light, were used for the evaluation of dark toxicity. Treated *P. gingivalis* was resuspended in phosphate-buffered saline and spread on blood agar plates. Cell viability was assessed by counting the colony-forming units after a 48 h incubation at 37° C under anaerobic conditions.

Results and Discussion

Approximately 99 percent of DOTAP:POPC liposomes, at a concentration of 100 µM lipid, were bound to *P. gingivalis*. Only 12.3 ± 7.1 percent of POPC:PG liposomes, and 18.1 ± 7.4 percent of POPC liposomes were bound (**FIGURE 1**). Thus, almost all the positively charged liposomes incubated with *P. gingivalis* were bound to the bacteria under these conditions. It would therefore be expected that all the photosensitizer molecules encapsulated in cationic liposomes would be localized at the surface of the bacteria (**FIGURE 2**).

Free zinc phthalocyanine at 5 and 10 µg/ml was partially toxic (10 percent and 22 percent, respectively) to *P. gingivalis* in the dark. When exposed to light, the cytotoxicity increased to about 30 percent and 35 percent, respectively (**FIGURE 3**). Zinc phthalocyanine could be encapsulated in DOTAP:POPC at 1 mole% without any apparent precipitation of the photosensitizer. Liposomal zinc phthalocyanine had a considerably higher cytotoxicity to *P. gingivalis* than free zinc phthalocyanine (**FIGURE 4**). At 5 µg/ml the toxicity was about 63 percent, and at 10 µg/ml it was approximately 77 percent. Control liposomes with the same lipid composition but without zinc phthalocyanine had approximately 20 percent dark- as well as light-toxicity (**FIGURE 4**).

Liposomes composed of a synthetic amphiphile, dioctadecyldimethylammonium bromide (DODAB), were shown to be toxic to *Escherichia coli*, *Salmonella typhimurium*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*, with the 50 percent toxic dose ranging from 28 to 5 µM.[11] Trafny et al.[12] reported that cationic liposomes containing ciprofloxacin or polymyxin B were effective in reducing the viability of *P. aeruginosa* on a matrix of human dermis, particularly when administered together. The minimum inhibitory concentration of cationic liposomes containing DOTAP and encapsulating meropenem were two to four times lower than the free drug

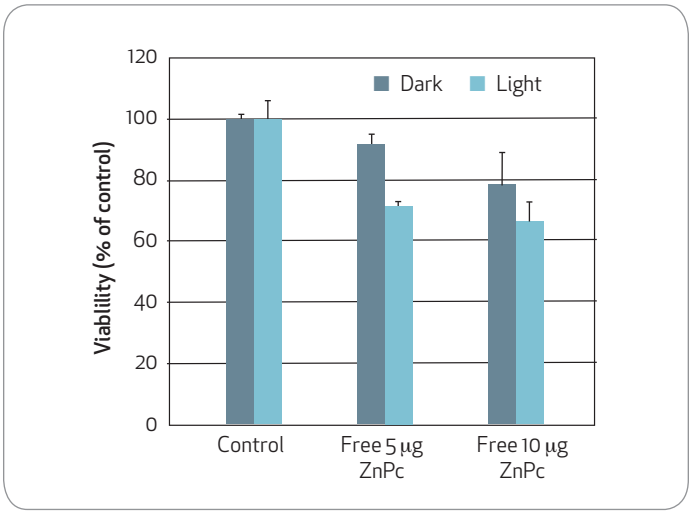

FIGURE 3. Bacterial viability following photoactivation of free zinc phthalocyanine. The data are given as the mean and standard deviation.

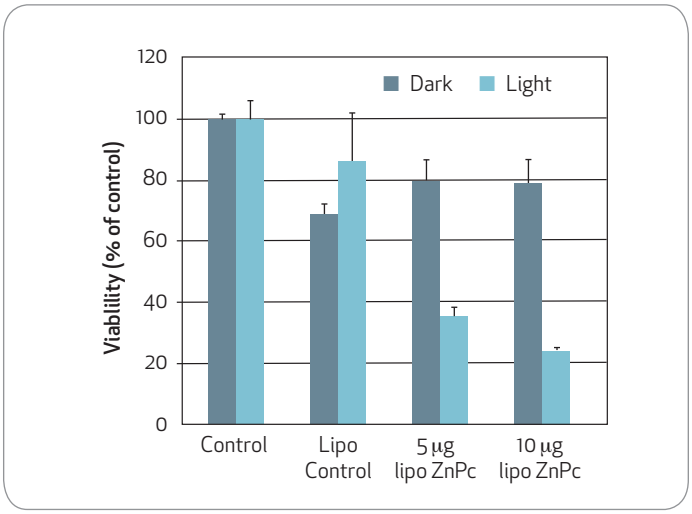

FIGURE 4. Bacterial viability following photoactivation of zinc phthalocyanine encapsulated in DOTAP:DOPC liposomes. The data are given as the mean and standard deviation.

against drug-susceptible *P. aeruginosa* strains.[13] The photosensitizer m-tetrahydroxyphenylchlorin encapsulated in mixed cationic liposomes composed of dimyristoylphosphatidylcholine and a cationic surfactant (7:3 molar ratio) was as effective in killing methicillin-resistant *Staphylococcus aureus* as free chlorin, both at a concentration of 10 µM.[14] Our results on liposome binding to *P. gingivalis* indicate that antibiotics encapsulated in cationic liposomes can be localized at the surface of the bacteria, and that the efficacy of certain antibiotics may be enhanced. These studies are ongoing in our laboratory.

The higher cytotoxic efficacy of zinc phthalocyanine in cationic liposomes suggests that such formulations can be utilized for localized delivery to the periodontal pocket and to plaque bacteria. Cationic liposomes are expected to retain the photosensitizer attached to the bacterial biofilm, providing a local reservoir over a prolonged period. It may also be possible to covalently couple antibodies to liposomes that can more specifically target the photosensitizer to cell surface components of *P. gingivalis* or other pathogenic bacteria. ■■■■

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THE CORRESPONDING AUTHOR, Alex Ko, can be reached at a_ko1@u.pacific.edu.

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Expression of EMMPRIN Modulates Mediators of Tumor Invasion in Oral Squamous Cell Carcinoma

AMANDA SIU, BS; JOY CHANG, BS; CASEY LEE; STACEY LEE, BS; CARLIN LEE, BS; AND DANIEL M. RAMOS, DDS, PHD

ABSTRACT Squamous cell carcinoma (SCC) accounts for 96 percent of all intraoral malignancies. The five-year survival rate is 50 percent and has not improved in 60 years. During SCC progression, subsets of SCC cells undergo an epithelial-to-mesenchymal transition (EMT) to become highly invasive. The extracellular matrix metalloproteinase inducer (EMMPRIN) contributes to EMT by activating local matrix metalloproteinases (MMPs). In this study, we found that EMMPRIN modulates the invasive phenotype and may be a potential therapeutic target.

AUTHORS

Amanda Siu, BS, is a fourth-year dental student at the University of California, San Francisco, School of Dentistry.
Conflict of Interest Disclosure: None reported.

Joy Chang, BS, is a second-year dental student at the University of California, San Francisco, School of Dentistry.
Conflict of Interest Disclosure: None reported.

Casey Lee is a fourth-year student at the University of California, Davis.
Conflict of Interest Disclosure: None reported.

Stacey Lee, BS, is a third-year dental student at the University of California, San Francisco, School of Dentistry.
Conflict of Interest Disclosure: None reported.

Carlin Lee, BS, is a graduate of the University of California, Irvine, and is applying to medical school.
Conflict of Interest Disclosure: None reported.

Daniel M. Ramos, DDS, PhD, is a professor of Oral Medicine at the University of California, San Francisco, School of Dentistry.
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Squamous cell carcinoma (SCC) accounts for 96 percent of all oral cancers. It is the sixth most common cancer and kills more than 8,000 Americans annually. The five-year survival rate is 50 percent and this prognosis has not changed in 60 years. At the time of diagnosis, 75 percent of patients present with regional metastasis, which reduces the five-year survival to 25 percent.[1,2]

Epithelial-to-mesenchymal transition (EMT) is a process in which cells lose their epithelial differentiation and acquire mesenchymal properties. EMT is a major facilitator of SCC invasion through the process of changing the expression, distribution and function of a number of proteins, including matrix metalloproteinases (MMPs), integrins and tenascin (TN-C).[3]

Interactions between primary SCC cells and the surrounding extracellular matrix (ECM) facilitate local invasion during the early stages of invasion.[4,5] As SCC progresses, the ECM is remodeled through a dynamic process involving the degradation of existing molecules coupled to the deposition of proteins responsive to an invasive niche. ECM remodeling involves the activation of MMPs and the neo-deposition of matrix molecules, such as TN-C. In general, MMPs modulate ECM homeostasis by maintaining the balance between deposition and degradation of specific matrix molecules. The extracellular matrix metalloproteinase inducer (EMMPRIN) facilitates tumor cell invasion by

inducing peritumor fibroblasts (PTF) to activate MMPs for matrix remodeling.[6] TN-C is a transitional ECM glycoprotein that is prominently expressed during wound healing and in certain tumors, such as SCC and glioblastoma. TN-C has anti-adhesive properties and is a ligand for the αvβ6 integrin.[6,7] One of the downstream events of TN-C-αvβ6 ligand binding is the activation of MMP3.

Tumor cell invasion is a complex process that involves the integrin family of cell surface adhesion receptors. Integrins allow interaction between tumor cells and the ECM. Thus, integrins modulate tumor cell invasion by providing direct links with the ECM, functioning as bidirectional transducers to extra- and intracellular signaling. Specific integrins are shown to be upregulated in different tumors. The αvβ3 integrin is expressed in invasive melanoma and the αvβ6 integrin is expressed in invasive epithelial tumors, including oral SCC.[6,7,8] Expression of the αvβ6 integrin is associated with EMT and poor prognosis in colon carcinoma.[9] We previously showed that the cytoplasmic domain of the β6 subunit is required for oral SCC cells to undergo EMT. The β6 subunit has an 11-amino-acid extension that is unique among integrin β subunits. When invasive oral SCC cells are transfected with a truncated β6 cDNA (missing the terminal 11 AA), the cells become noninvasive, regain a polarized state and reexpress E-cadherin. This suggests that the full-length β6 cDNA suppresses the well-differentiated epithelial phenotype and promotes the poorly differentiated mesenchymal phenotype.

Our past research shows that the αvβ6 integrin complexes with Fyn and EMMPRIN.[10,11] The stability of these complexes depends upon the presence of the full-length β6 cytoplasmic tail.[11] The complex formation activates focal adhesion kinase (FAK) and the mitogen-activated protein (MAP) kinase pathway, which promotes tumor growth.[10] Tumor growth is oxygen dependent. Without a new influx of blood vessels, a tumor will not thrive beyond 3-5 mm. In an oxygen-limited environment, some tumors have developed an alternative mechanism of neovascularization termed "vascular mimicry."[12] Tumors create their own tumor cell-lined channels for fluid transport independent of typical modes of angiogenesis. These tumor cell-lined conduits may express endothelial-selective markers and anticoagulant factors, which allow for anastamosis with host endothelium. Our previous work has shown that β6-positive SCC cells are capable of forming vascular channels both in vitro and in vivo.[13] Under hypoxic conditions, the transcription factor, hypoxia inducible factor-1α (HIF-1α), activates lysyl oxidase (LOX). LOX initiates covalent cross-linking of collagen and elastin, providing the tensile strength in the ECM that is important in invasion.[14]

In this study, we evaluate how the expression of EMMPRIN can alter and promote the invasive phenotype of oral SCC cells.

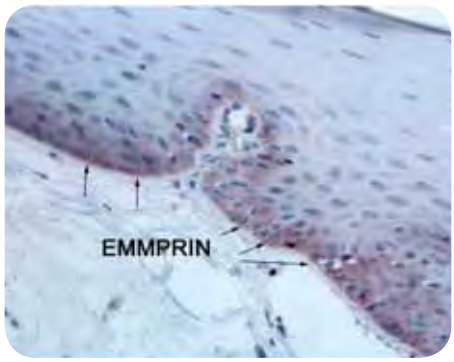

FIGURE 1A.

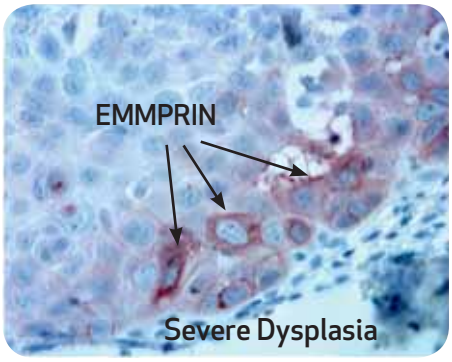

FIGURE 1B.

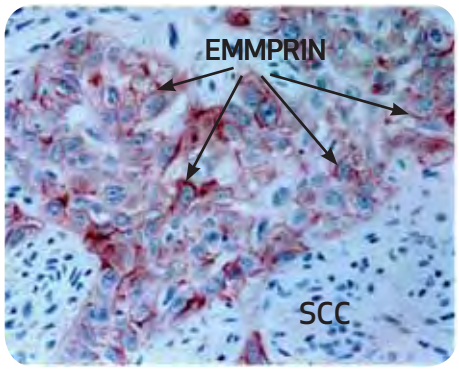

FIGURE 1C.

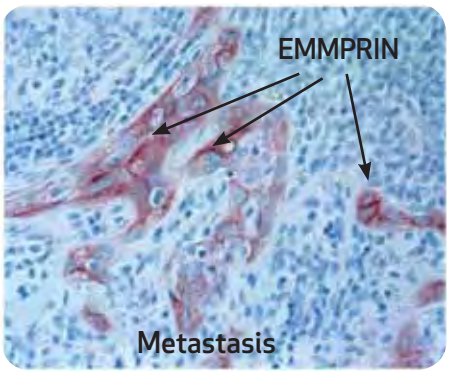

FIGURE 1D.

FIGURES 1. EMMPRIN expression is elevated in primary and metastatic SCC lesions. Biopsy specimens from normal oral mucosa (**A**), dysplastic oral mucosa (**B**), oral SCC primary tumor (**C**) and a metastatic lesion (**D**) were evaluated by immunohistochemistry using antibodies to EMMPRIN. In normal mucosa, EMMPRIN was almost exclusively located in the basal cell layer. In dysplasia, EMMPRIN was expressed in the basal layer and in the next three to four cell layers suprabasally. In both the primary and metastatic lesions, EMMPRIN was localized to the cell membrane throughout the entire lesion. These results indicate a progressive increase in the expression of EMMPRIN as normal tissue progresses to dysplasia and oral SCC.

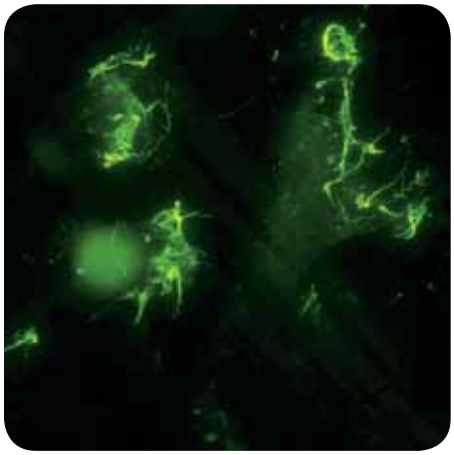

FIGURE 2A.

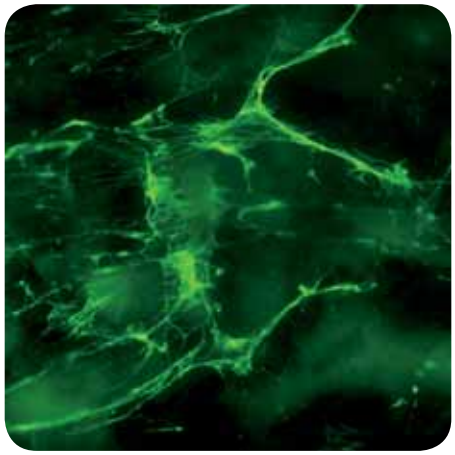

FIGURE 2B.

FIGURES 2. Organization of a TN-C three-dimensional matrix is modulated by EMMPRIN. Oral SCC9 cells were co-cultured for 24 hours with peritumor fibroblasts (PTF) under serum-free conditions to mimic in vivo interactions. The SCC9/PTF co-cultures produced a sparse TN-C three-dimensional matrix (**A**). In contrast, the SCC9HE/PTF co-cultures produced a rich, dense, highly organized TN-C matrix (**B**). This indicates EMMPRIN plays a prominent role in organizing a three-dimensional TN-C matrix.

Materials and Methods

Cell Culture

Oral SCC9 (derived from a tongue lesion) and SCC9SN (vector only) were obtained from James Rheinwald, PhD, Brigham and Woman's Hospital, Harvard School of Medicine and have been discussed elsewhere.[15] Transfecting SCC9 cells with the blank viral vector created the SCC9SN cell line. Expressing full-length EMMPRIN cDNA into the poorly invasive, β6-negative SCC9 cells produced the SCC9HE cell line. Peritumor fibroblasts (PTF) were isolated from a biopsy of an oral SCC lesion. The bulk of the specimen was submitted for pathology and 1 mm of tissue was used to isolate PTF. The tissue was plated in Dulbecco's Modified Eagle's Medium (DMEM) and the PTF were allowed to migrate out from the tissue. PTF were verified by the expression of vimentin and the absence of cytokeratins. All cells were cultured in DMEM with 10% fetal bovine serum, nonessential amino acids and 2% Vitamin Solution (Life Technologies, Grand Island, N.Y.). SCC9, SCC9SN and SCC9HE cell lines were grown in normal growth conditions (humidified atmosphere at 37° C, 5% CO_2). For hypoxia experiments, SCC9 and SCC9HE cells were incubated in an airtight anaerobic incubator (1% O2 with 94% N2 and 5% CO_2) for 24 hours. Matrigel was purchased from BD Biosciences (San Jose, Calif.).

Antibodies

Rabbit polyclonal antibodies to EMMPRIN (34-5600) were purchased from Zymed Laboratories Inc. (South San Francisco, Calif.). Rabbit polyclonal antibodies to HIF-1α were purchased from Cell Signaling Technology Inc. (Danvers, Mass.). Rabbit polyclonal antibodies to LOX were purchased from Santa Cruz Biotechnology Inc. (Dallas). Mouse monoclonal antibodies to TN-C (BC-4) were a gift from Luciano Zardi, PhD (Instituto Nazionale, Genoa, Italy). Mouse monoclonal antibody to αvβ6 (10D5) was a generous gift from Dean Sheppard, MD (UCSF).

Co-cultures

Co-cultures of PTF and SCC cells (1:1 ratio) were seeded in the presence of 1% serum for 60 minutes to allow the cells to adhere. The serum was aspirated and replaced with serum-free DMEM. The cultures were grown for 48 hours and then processed for immunofluorescence microscopy using antibodies to TN-C.

Immunohistochemistry

Frozen biopsy specimens from normal oral mucosa, dysplasia, primary SCC and metastatic lesions were obtained from UCSF Oral Pathology. The tissue was incubated in the presence of polyclonal antibodies to EMMPRIN (Zymed, 34-5600) overnight at room temperature and then processed for routine immunohistochemistry.[16]

Western Blotting

Cells were serum starved for 24 hours and then plated onto 10 μg/ml of fibronectin (FN) for two hours. Cells were lysed in Nonidet P-40 lysis buffer (150 mM NaCl, 1 mM EDTA, 20 mM Tris-HCl, pH 7.5, 50 mM NaF, 1 mM Na3VO4, 0.1% Nonidet P-40, 10μg/ml leupeptin, 0.05% aprotinin, 1 mM phenylmethylsulfonyl fluoride). Protein concentration was determined by BCA Protein Assay Kit (Pierce Biotechnology, Rockford, Ill.). The proteins were separated using SDS-PAGE and transferred to PVDF membrane (EMD Millipore Corp, Billerica, Mass.) on semidry blotting apparatus (Bio Rad, Hercules, Calif.). The immunoblots were visualized using the Pierce ECL Western Blotting Substrate (Pierce Biotechnology) and UltraCruz Autoradiography Film (Santa Cruz Biotechnology Inc.). Blots were quantified and assigned relative value units (RVUs) using an image analysis program (NIH image).

Angiogenesis Assay

SCC9 cells and SCC9HE cells (2×10^5) were plated on a thin layer of Matrigel under serum-free conditions for 24 hours. To evaluate the putative role of MMPs in channel formation SCC9HE cells were incubated with the protease inhibitor GM6001. The cultures were then examined for channel formation using phase-contrast microscopy.

Tumor Growth in Mouse Models

2x10^6 SCC9 and SCC9HE cells in a 50 µl volume of serum-free medium were inoculated into the hind flank or footpad of athymic mice. The mice were monitored daily for ambulatory and food intake ability. The tumors were allowed to develop and grow until the tumor reached between 5 mm and 1 cm. After four weeks, the animals were sacrificed and subjected to necroscopy. Tumors were harvested, weighed and processed for routine immunohistochemistry.

Results

EMMPRIN expression is increased in oral SCC. Tissue specimens of normal, dysplastic, primary SCC tumors and metastatic lesions were evaluated using immunohistochemistry for the expression of EMMPRIN. EMMPRIN expression in normal oral mucosa was localized to the basal cell layer, which confirmed our previous results (**FIGURE 1A**).[16] In dysplasia, EMMPRIN expression was in the basal cell layer and extended several layers suprabasally (**FIGURE 1B**). In contrast, the epithelium of primary SCC tumors and metastatic lesions were stained entirely positive for EMMPRIN (**FIGURE 1C** and **1D**). This suggests EMMPRIN expression becomes dysregulated as oral mucosal tissue transforms to dysplasia, moderate dysplasia, primary SCC and metastatic lesions. The unrestricted expression of EMMPRIN may provide individual SCC cells with the competency to break away from the rest of the epithelial sheet and invade the surrounding tissue.

Expression of EMMPRIN increased remodeling of a three-dimensional TN-C matrix. The microenvironment surrounding tumor cells plays an important role in cancer progression. The ECM can be characterized by its distribution (cell-associated versus deposited), composition and source (tumor or stromal cells). In this study, we evaluated the deposition of TN-C using a co-culture system (SCC/PTF) to mimic the in vivo microenvironment. PTF cells were co-cultured with SCC9 or SCC9HE cells for 24 hours and analyzed for deposition of TN-C. The TN-C matrix organized by the SCC9/PTF cultures was sparse and barely detectable (**FIGURE 2A**). In contrast, the SCC9HE/PTF cultures had a robust TN-C matrix (**FIGURE 2B**). This suggests that the ECM deposited by the SCC9HE co-cultures was modulated by the presence of EMMPRIN.

EMMPRIN modulates αvβ6 expression. The αvβ6 integrin is a multifunctional epithelial-specific integrin whose ligands include FN, TN-C and the latency associated peptide (LAP) of TGFβ1. The αvβ6 integrin is a major factor influencing oral SCC invasion. We evaluated αvβ6 expression in the SCC9HE cells, the β6-negative SCC9 cells and the β6-positive SCC9 β6 cells.[10] The three cell lines were suspended, washed with PBS, incubated with 10 µg/ml of 10D5 overnight and then processed for flow cytometry. Our results show that β6 expression in SCC9HE was at least 30-fold greater than expression in the parental SCC9 (**FIGURE 3**). These results demonstrate a unique role for EMMPRIN in promoting the invasive phenotype by upregulating the expression of the β6 integrin.

Expression of EMMPRIN promotes vascular mimicry. Successful tumorigenesis requires a constant supply of oxygen. In the absence of neovascularization, some tumors form their own vessel-like structures in a process called vascular mimicry. Our lab previously showed that vascular-like channels are formed by the SCC cells expressing the αvβ6 complex in vitro and in vivo.[12,17] In this study, we

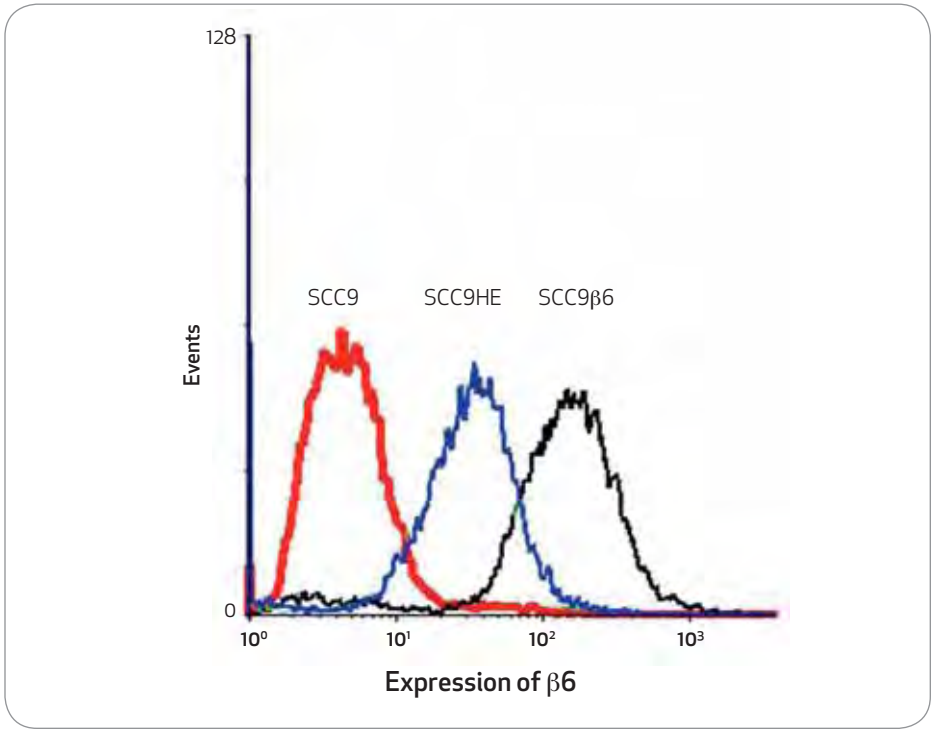

FIGURE 3. Expression of EMMPRIN results in an upregulation of the β6 integrin. The SCC9, SCC9HE and SCC9β6 cells were evaluated for the expression of the β6 integrin. The cells were removed from the tissue culture plates by a light treatment with EDTA, rinsed with PBS and incubated overnight with antibodies to αvβ6. The cells were processed for flow cytometry and evaluated for the expression of αvβ6. As previously shown, the SCC9 cells express little β6 integrin. In contrast, β6 expression in the SCC9HE cells was approximately 30 times greater than the SCC9 cells. The positive control, SCC9 β6 cells, expressed more than 50-fold greater levels of the αvβ6 complex compared to the SCC9 cell line.

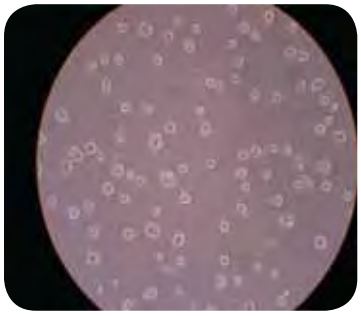

FIGURE 4A. SCC9

FIGURE 4B. SCC9HE (-)

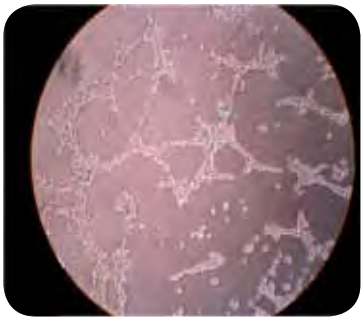

FIGURE 4C. SCC9HE (+)

FIGURES 4. Expression of EMMPRIN promotes vascular mimicry in vitro. To evaluate vascular mimicry, we seeded 2x10^5 SCC9 (**A**) and SCC9HE cells (**B**) on Matrigel for 24 hours to evaluate growth using our previously described assay. The SCC9HE cells were also incubated in the presence of 10 μM of a broad-spectrum protease inhibitor, GM6001 (**C**). After 24 hours, the SCC9 cells (**A**) remained as single isolates, whereas the SCC9HE (**B**) cells formed interconnecting networks resembling nascent blood vessels (vascular mimicry). When the SCC9HE cells were incubated with GM6001, network formation was partially suppressed (**C**). This demonstrates that EMMPRIN promotes channel formation and the suppression of these channels by GM6001 implicates MMP activity in this process.

examined if EMMPRIN-expressing cells possessed vascular mimicry capability. We compared the growth of the SCC9 and the SCC9HE cells seeded on a Matrigel matrix under serum-free conditions for 24 hours. The cultures were then gently fixed with paraformaldehyde and evaluated for channel formation using phase-contrast microscopy. The SCC9 cells remained either as single-cell isolates or spherical clusters with no lamellapodia or pseudopodia (**FIGURE 4A**). In contrast, SCC9HE cells formed extensive remodeling and interconnecting channels (**FIGURE 4B**). The channels formed by the SCC9HE cells resembled leaky blood vessels. To verify the role of MMPs in this process, we incubated the SCC9HE cells with GM6001, a nonspecific extracellular matrix metalloproteinase inhibitor. The formation of the channels was drastically suppressed with GM6001 (**FIGURE 4C**). This suggests that EMMPRIN promotes matrix remodeling and channel formation through MMP activation.

Expression of EMMPRIN in SCC cells upregulates HIF-1α. Oxygen is a constant requirement for tumor growth. Vascularization is required for tumor growth beyond 3-5 mm in size. The transcription factor HIF-1α is an important component in response to oxygen deprivation. HIF-1α promotes EMT by decreasing the expression of E-cadherin and suppressing the epithelial phenotype. We examined the expression of HIF-1α in SCC9 and SCC9HE cell lines grown under normal and hypoxic conditions for 24 hours. The expression of HIF-1α was slightly higher in the SCC9HE cells than in SCC9 cells under normal growth conditions. Under hypoxic conditions, a pronounced increase in HIF-1α expression was seen in the SCC9HE cells, but not in the SCC9 cells (**FIGURE 5**).

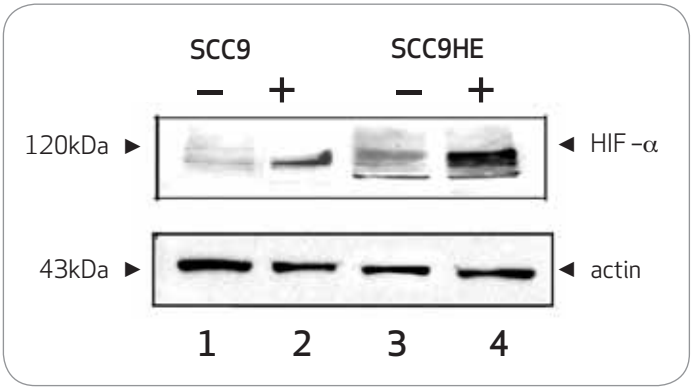

FIGURE 5. Hypoxia inducible transcription factor-1 (HIF-1) is induced by EMMPRIN expression. SCC9 (lanes 1, 2) and SCC9HE cells (lanes 3, 4) were plated on fibronectin under normal growth conditions (-) (humidified atmosphere at 37°C, 5% CO_2) or subjected to conditions of hypoxia (+) (1% O_2 with 95% CO_2, 94% N_2) for 24 hours in an airtight anaerobic incubator. The cells were lysed and processed for Western blotting using antibodies to HIF-1α. Antibodies to actin were used as loading controls. Note the pronounced increase in HIF-1α under conditions of hypoxia in the SCC9HE cells (lane 4). SCC9 cells show a slight increase in HIF-1α expression under hypoxic conditions (lane2).

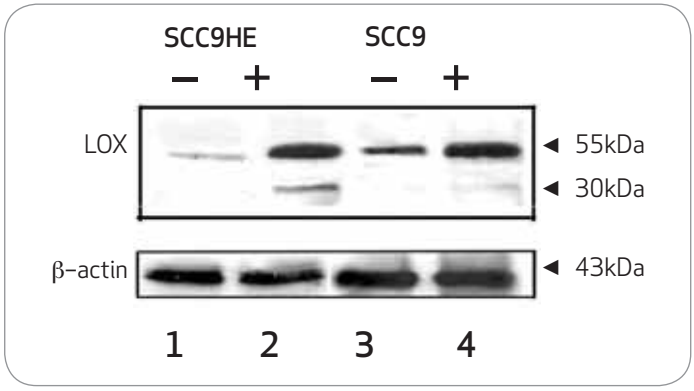

FIGURE 6. Expression of EMMPRIN promotes expression of LOX. One of the downstream targets of HIF-1α is lysyl oxidase (LOX). SCC9HE (lanes 1, 2) and the SCC9 (lanes 3, 4) were grown for 24 hours serum-free under normal conditions of 5% CO_2 (-) or under hypoxic conditions (+), and the conditioned medium was collected, concentrated and evaluated by Western blotting for the expression of LOX. The SCC9 cell-conditioned medium-expressed low levels of the LOX precursor. In contrast, the SCC9HE cell-conditioned medium-expressed high levels of the 55 kDa precursor, as well as the 30 kDa mature form of the molecule. These results suggest that EMMPRIN promotes the expression of LOX in oral SCC cells.

These results indicate that EMMPRIN has a multifactorial role in the invasive process and contributes to the invasive phenotype by upregulation of HIF-1α.

Upregulation of LOX in EMMPRIN expressing SCC cells. In the ECM, LOX initiates cross-linking of collagens and elastin. LOX is secreted into the ECM as a pro-enzyme and is activated by hypoxia partially by HIF-1α and TGFβ1. Clinically, patients with elevated LOX typically have poor survival. To evaluate the potential role of LOX in oral SCC we performed Western blotting on the conditioned medium from the SCC cell lines. Each cell line was grown under normal and hypoxic conditions and after 24 hours, the culture media was collected and then analyzed by Western blotting for expression of LOX. Under aerobic conditions, the conditioned media from both cell lines contained relatively high levels of the inactive, precursor form of LOX (50 kDa). Under anaerobic growth conditions, the mature form of LOX (30 kDa) was detected in the conditioned medium from the SCC9HE cells and not the SCC9 cells (**FIGURE 6**). This demonstrates that in response to oxygen deprivation, the SCC9HE cell line has the ability to activate LOX and promote the invasive phenotype.

Expression of EMMPRIN promotes tumor growth and distant lesion formation. To evaluate how EMMPRIN expression affects tumor growth and behavior, we performed an in vivo tumor growth assay. For tumor cells to spread, they need to intravasate into a vessel to gain access to the blood stream. At a distant site, the tumor cells must arrest in a vessel and physically cross the vessel walls. An in vivo model is required to truly analyze this process. We inoculated $2x10^6$ SCC9 and SCC9HE cells into the hind flank of six athymic mice per condition. The mice were monitored daily for overall health and their ability to eat and drink. The tumors were allowed to develop for four weeks. The animals were sacrificed and the tumors were weighed. Tumors formed by the SCC9HE cells were 10-fold larger than those formed by the SCC9 cells (**FIGURES 7A** and **7B**). We also were interested in determining whether the expression of EMMPRIN provided tumor cells with the capacity for metastasis. We performed footpad injections to evaluate this phenomenon. $2x10^6$ SCC9 and SCC9HE cells were injected into the footpad of six athymic mice per condition. The animals were monitored daily to ensure they were not distressed. After four weeks, the animals were evaluated and sacrificed.

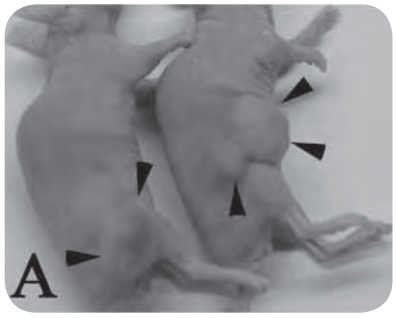

FIGURE 7A. SCC9HE

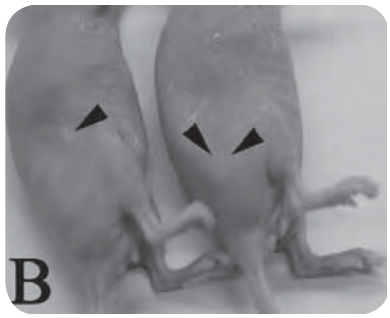

FIGURE 7B. SCC9

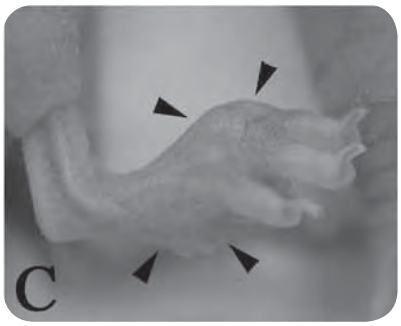

FIGURE 7C. SCC9HE

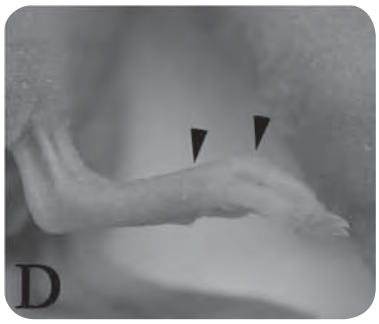

FIGURE 7D. SCC9

FIGURE 7E. Axial node (SCC9HE)

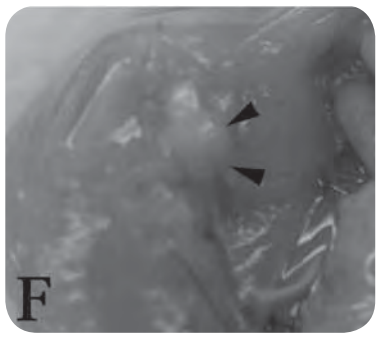

FIGURE 7F. Axial node (SCC9HE)

FIGURES 7. Expression of EMMPRIN promotes tumor growth and distant lesion formation. To evaluate how EMMPRIN expression may influence tumor growth and invasion, $2x10^6$ SCC9 or SCC9HE cells in a 50 µl volume of serum-free medium were injected into the hind flank of nu/nu mice. At four weeks, the size of the primary tumor generated by the SCC9HE cells was more than 10-fold larger than those formed by the SCC9 cell line (**A** and **B**). Similarly, when injected into the footpad of nu/nu mice, the tumor formed by the SCC9HE cells was almost five-fold larger than the tumors formed by the SCC9 cells (**C** and **D**). Additionally, two of the six animals developed distant lesions to the axial nodes (**E** and **F**). These results indicate that the overexpression of EMMPRIN can promote tumor cell growth and possible distant metastases. In **7G** the histogram represents the hind flank and footpad lesions by weight. The hind-flank tumors generated by SCC9HE cells average 7 grams. The tumors formed by SCC9 cells average 1 gram. The footpad lesions formed by the SCC9HE cells average 1 gram and SCC9 cells generated lesions average less than 0.1 gram.

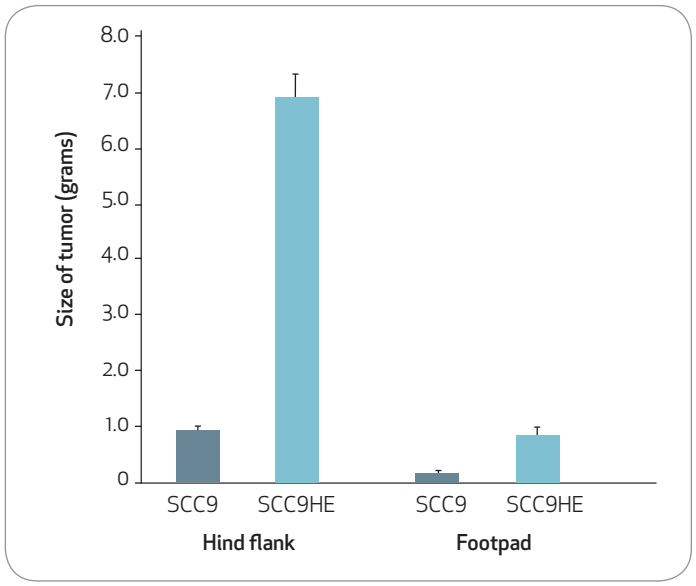

FIGURE 7G. Lesions by weight

The tumors formed by injection of the SCC9HE cells were five-fold larger than those formed by the SCC9 cells (**FIGURES 7C** and **7D**). When the animals were analyzed by necroscopy, two of the animals injected in the footpad with SCC9HE cells developed a distant lesion in the axillary lymph node region (**FIGURES 7E** and **7F**). The tumors generated by injecting the SCC9HE cells into the hind flank weighed on average about 7 grams; whereas tumors generated by the SCC9 cells weight less than a gram (**FIGURE 7G**). The SCC9HE cells injected into the mouse footpad generated metastatic lesions and formed primary lesions that weighed 1 gram. The SCC9 cells formed primary tumors of less than 1 gram. These results indicate that the expression of EMMPRIN by SCC cells promotes localized, enhanced tumor growth and induces the formation of metastasis.

Discussion

The five-year survival for SCC of the oral cavity is 50 percent and this prognosis has not changed in 60 years. The incidence of SCC comprises approximately 6 percent of all cancers, but the morbidity and mortality associated with this disease outweighs its incidence. Factors that contribute to the high mortality of SCC include late detection, proximity to vasculature and lymphatic drainage, local invasion, recurrence and metastasis. The understanding of SCC behavior is essential to create improved therapeutic approaches.

Our previous work showed that upregulation of the αvβ6 integrin, TN-C and EMMPRIN occur simultaneously and contributes to the invasive profile of SCC.[6,13] The subset of SCC cells that expresses the αvβ6 integrin initiates EMT by providing those cells with an invasive advantage over αvβ6-negative SCC cells. The αvβ6 positive SCC cells establish an invasive niche through the increased deposition of TN-C. The shift to a TN-C rich matrix is known to promote invasion and metastasis.[10] TN-C binding to the αvβ6 integrin forms a physical complex between the cytoplasmic domain of the β6 integrin, Fyn kinase and FAK. The stability of this complex is dependent upon the presence of the complete β6 cytoplasmic domain. In addition, we previously demonstrated that EMMPRIN is a component of this complex and its formation triggers a variety of intracellular signaling events including the activation of the RAF/RAS/MAPK pathway.[11]

In the current study, we defined an EMMPRIN expression profile in tissue sections from normal oral mucosa, dysplasia, primary SCC and distant metastasis. In normal tissue, EMMPRIN expression is restricted to the basal cell layer. However, EMMPRIN expression levels and localization are significantly altered in primary SCC and in metastatic lesions. This suggests that EMMPRIN may cause a disruption in cell-cell junctions, which is a characteristic associated with EMT.

In vivo, tumor cells grow intimately with the ECM and resident fibroblasts. In this study, we used a co-culture system, consisting of SCC cells and PTF, to examine TN-C deposition. SCC cells that overexpress EMMPRIN were compared to the SCC cells that poorly express EMMPRIN. We found that co-cultures containing SCC9HE/PTF cells deposit a rich, highly organized TN-C matrix. In contrast, the SCC9/PTF cultures organized a very thin, delicate TN-C matrix, indicating that pre-enzymatic modification may be required prior to deposition of TN-C into a matrix. We also determined that the SCC9HE cells express αvβ6, which we previously determined is a requirement for induction of TN-C into a matrix.[7,18] Our results suggest that EMMPRIN, the αvβ6 integrin and TN-C interact closely and have bidirectional effect upon one another. The interaction between these molecules is important for tumor progression.

Understanding how solid tumors grow under conditions of hypoxia has been a major obstacle in designing therapeutic strategies. During embryogenesis, vasculogenesis can occur by the differentiation of mesodermal progenitor cells into a primitive vascular network.[19] Angiogenesis, the development of new vessels from preexisting capillaries, occurs through remodeling of the

primitive vascular networks.[19] Similarly, tumorigenesis requires the formation of new blood vessels. In our study, we found that the tumor cells overexpressing EMMPRIN are able to form networks of channels when placed into a three-dimensional matrix. These channels resemble primitive blood vessels and are partially aborted using a broad-spectrum protease inhibitor. This suggests that under the right conditions, EMMPRIN-expressing oral SCC cells can initiate vascular mimicry mediated by MMP activation. Tumor hypoxia promotes accumulation of HIF-1α, which has a significant effect on tumor progression and metastasis.[20] We show that HIF-1α expression is upregulated by the expression of EMMPRIN. EMMPRIN also promotes expression of LOX, a downstream target of HIF. LOX modifies and stabilizes the ECM, thus enhancing tumor cell invasion and proliferation. Therefore, EMMPRIN promotes the expression of HIF, which activates the LOX-induction of Snail, an important E-cadherin repressor.

β-catenin associates with E-cadherin at cell-cell junctions and serves as a transcription factor for the Wnt pathway.[21] When EMMPRIN downregulates E-cadherin expression, β-catenin is able to access the nucleus and contribute to the Wnt pathway. Wnt contributes to EMT through the downregulation of E-cadherin, thus promoting the invasive and metastatic phenotype.

To evaluate tumor cell behavior in vivo, we performed both growth and metastasis assays in athymic mice. When EMMPRIN-expressing SCC cells were inoculated in athymic mice, their growth outpaced that of the EMMPRIN-negative cells. The tumors formed by the SCC9HE cells were between five- and 10-fold larger than those formed by the SCC9 cell line. Additionally, the SCC9HE cells formed a distant metastatic lesion when injected into the footpad of the animal.

Overall, we found that EMMPRIN promotes the invasive phenotype by allowing the cells the freedom to progress through EMT. The tumor cell interactions we described are crucial to successful tumor growth, formation of vessel-like structures and eventual metastasis. The process of tumor invasion and metastasis is influenced by the interactions between the ECM and the cytoskeleton. The cytoskeleton reorganizes as a result of extracellular signals transmitted via the cytoplasmic domain of integrin receptors. Our previous work showed that the cytoplasmic domain the of the integrin β6 physically complexes with EMMPRIN. In this study, we further characterize EMMPRIN and show how EMMPRIN contributes to the invasive process. Understanding the mechanisms of EMMPRIN-induced cell invasion may present opportunities for new therapeutic treatments in head and neck SCC. ■■■■

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THE CORRESPONDING AUTHOR, Daniel M. Ramos, DDS, PhD, can be reached at daniel.ramos@ucsf.edu.

CDA JOURNAL, VOL 41, Nº11

Segmenting the Business of Dentistry

MICHAEL PERRY, DDS

Dentists are in large measure applied scientists, favoring an evidence-based, objective approach to decision making. Business management principles in general are based in the social sciences — economics, psychology and sociology. These sciences are more theoretically based than the chemistry, physics and physiology that underpin the clinical side of what dentists do.

To make the business of dentistry easier for the linear-thinking dentist to study and master, it is helpful to separate the subject matter into 10 segments: Three "foundational" issues and seven "systems" issues.

The foundational issues are Envisioning, Leadership and Strategic Planning of Continuing Education. These are interwoven in a way where a change with one issue will often demand changes with the other two.

The systems issues are Pricing, Patient Scheduling, Financial Policy, Case Presentation, Overhead Control, Employee Incentives and Marketing. Each of these systems can be improved either independently or in conjunction with the others.

There are numerous subgroups of each of these 10 segments. These segments and their subgroups will be discussed in future articles.

Today's Marketplace

The dental marketplace is a subgroup of the general marketplace. It in turn is a conglomerate of many submarkets such as dental benefits, technology and labor, to name just a few.

The large majority of CDA members practice on a for-profit basis either as practice owners or as associate employees. Their work in the dental marketplace is affected by forces, known and unknown, that alter the submarkets. Both the demand for dental services and the price of dental services can change as a result of these processes.

Fundamental Change

Since 1979, dentists have experienced many fluctuations in the dental marketplace that have affected the business of dentistry. These have certainly included changes in general demand commensurate with the rise and fall of the business cycle. They have also included changes in technology such as the improvements in dental implants and adhesives. In addition, there have been changes in the labor market, such as the shortage of dental hygienists that occurred in the 1990s and the apparent excess number of dental hygienists that exists in some parts of California today.

In his classic business book, *Only the Paranoid Survive*, Andrew Grove declares his tenet that "sooner or later something fundamental in your business world will change." He tells the story of his experience as chair of the board of Intel Corp. when the silicon microchip was replacing the transistor. Two such fundamental changes have occurred in the dental business world in the past half century.

The first occurred in 1954 when the Washington Dental Service (Delta Dental of Washington) had its genesis as the first dental benefits company. The California Dental Service followed in 1955. This initiated the age of subsidized private-sector dental care where third parties paid a substantial percentage of the cost of treatment. Dental benefit companies sold plans to employers that allowed dentists to charge patients at or near market rates even when the dentist contracted directly with the dental benefits company. These market rates have come to be known as "usual, customary and reasonable" (UCR). Today, the majority of dentists in California have one or more of these contracts.

The second fundamental change is occurring now. Market forces have changed to where employers, in general, are no longer willing to pay the premiums necessary to purchase the types of benefit plans they had in the past. Plans with fee schedules substantially below UCR now dominate the dental benefits marketplace.

Survey data shows that the changing dental benefits marketplace is CDA members' No. 1 concern. The next Practice Support column will define the marketplace that exists today and describe strategies for doing business in this marketplace. ■■■■

Michael Perry, DDS, is currently a member of the California Dental Association Council on Membership and the Dental Benefits Research Task Force. He is also the chair of the CDA Practice Support Center Task Force. Dr. Perry is a practicing general dentist in Santa Rosa and a dental business consultant.

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A look into the latest dental and general technology on the market.

iPhone 5s (Apple Inc., $199 for 16GB with contract, $299 for 32GB for contract, $399 for 64GB with contract)

On Sept. 20, Apple released the latest version of its iPhone line of smartphones, the iPhone 5s. Although the "s" denotes an incremental update to the previous iPhone 5, this latest model definitely offers some impressive new features and functionalities. While the overall design and form factor of the phone remains unchanged from the iPhone 5, quite a few changes have been made "under the hood." Most notably, the 5s has a "Touch ID" fingerprint identity sensor built into the Home button of the phone, providing a much faster and (arguably) more secure option than having to enter a number-based passcode. In practice, the Touch ID is simple to set up and flawless to use, allowing much easier access than previous iPhones. It also offers the additional benefit of being able to make purchases from the iTunes and App Stores with just a quick scan of the thumb. The built-in camera has also received a significant upgrade. The iSight camera's sensor has been increased by 15 percent, ostensibly improving the overall quality of photographs by increasing the size of the actual pixels captured. "Continuous burst mode" lets users take 10 photos per second simply by holding down the shutter button, which users can then quickly go through, select their favorites and delete all of the remaining photos with a single click. A dual white and amber LED provides a vastly improved flash, improving the overall quality of images captured, especially in dimly lit situations. Finally, the ability to capture slow-motion, high-definition video is both impressive and incredibly entertaining. Other improvements have been made, such as including a 64-bit processor (delivering desktop-class speeds), a new coprocessor tracking every type of motion (which knows when the user is walking, running or driving) and making the phone available in new colors such as gold and silver. Although this review of the 5s was completed after less than a week of use, so far it has truly impressed with both the overall functionality as well as the aesthetics.
—Blaine Wasylkiw, director of online services, CDA

Chromecast (Google, $35)

Chromecast is an adapter that connects to any high-definition television with an HDMI port and streams audio/video content from a Wi-Fi enabled local network. Content available for streaming includes YouTube, Netflix, Google Play Music and Google Play Movies and TV. Chrome browser sessions can also be mirrored to the device for display on the TV and include audio and video. The adapter attaches directly to the HDMI port of a TV. An optional extension cable is included if the adapter size prevents connection. The adapter must also be connected to a power source via an included micro-USB-to-USB cable. This cable connects the micro-USB port of the Chromecast to a powered USB port on the TV or through an included external power supply. Setup of Chromecast is easy. Once the TV input is switched to the adapter, users download a setup app on any Wi-Fi-enabled Mac, PC, Chromebook Pixel, Android or iOS device. Launching the app will create an ad hoc Wi-Fi network that the Chromecast uses for the setup process. Users select their local Wi-Fi network, enter their network password and the setup is complete. Users will see a Chromecast icon on all content that can be streamed. Clicking the icon makes the content appear on the TV. With the exception of streaming a Chrome session, once content is casted, the original device is no longer needed as Chromecast is streaming directly from the Internet. YouTube and Netflix work with all supported platforms, which include Mac, PC, Chromebook Pixel, Android and iOS. Google Play content streaming is limited to Android. Chrome sessions support Mac, PC or Chromebook Pixel with an installed extension. Users are able to mirror content from sites such as Hulu and Pandora from a Chrome session stream. With its relatively low price point, Chromecast is a welcome addition to any TV as a media hub device.
—Hubert Chan, DDS

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Dentists interested in contributing to this section should contact Tech Trends Editor Blake Ellington at blake.ellington@cda.org.

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PACOIMA - Leasehold &Equipment Only! Two eq op w/ 1 plmbd not eq office in small strip mall. Charts included. ID #4361.
RESEDA - GP located on a single story bldg w/ heavy traffic flow. 18 year of gdwll. 5 eq operatories. Some Ortho. Net $235K. ID#4333.
TORRANCE (GP) - Modern designed office w/ 44 yrs of gdwll. Has 3 eq ops, 1 plmbd not eq w/ digital x-ray & Eaglesoft soft. ID#4375.
TORRANCE - GP w/ over 30 yrs of gdwll in 2 story prof med bldg. Consists of 8 eq ops, 1 plmbd not eq in 2,208 sq ft suite. ID #4377.
TORRANCE - Free for service turn-key practice in busy shopping center. Heavy foot traffic. Modern decor office w/ 3 eq ops. ID #4391.
WESTWOOD VILLAGE - With over 70 yrs of gdwll this practice consists of 4 eq ops in a 2 story prof bldg. Net $266K. ID #4401

ORANGE COUNTY

DANA POINT - Leasehold & Equip Only! Located in a 2 story dent/med bldg. Consists of 5 eq ops in a 1,200 sq ft ste. ID #4397.
HUNTINGTON BEACH (GP) - Fee for service practice w/ 3 eq ops, 3plmbd not eq in a 2,100 sqft ste on a busy street. ID#4395.
MISSION VIEGO (GP) - Well designed turn-key practice w/ 3 eq op & 3 plmbd is located in a prestigious shopping center. ID #4303.
SAN CLEMENTE (GP) - Modern designed turn-key office in 2 story med bldg w/ 4 eq ops, 2 plmbd not eq for expansion. ID 4359.

RIVERSIDE / SAN BERNARDINO COUNTIES

APPLE VALLEY (GP) - Well established practice w/ 5 eq op, 3 plmbd not eq, Dentrix software and digital x-ray. Net $214K. ID #4349.
BANNING - Leasehold & Equip Only! Modern designed practice w/ 3 eq ops in 1 story prof bldg. Remodeled in 2011. ID #4117.
BARSTOW(GP) - Long established office w/ 4 eq ops in a single story bldg. Easy freeway access. Fee for service. ID #4241
FONTANA (PEDO) State of the Art practice located in 1 story multi use bldg with 2 eq ops / 3 chair in open bay. 85% Denti-calID #4301.
PALM DESERT (GP) - Well established practice w/ 5 eq ops in 1 story bldg w/ ample parking & excellent signage. Net $119K. ID#4331.
PALM SPRINGS - Leasehold & Equip Only! Practice located on a busy street w/ 4 eq ops in a 2,000 sq ft office. ID #4387.

SAN DIEGO COUNTY

CHULA VISTA (GP) - Located in downtown. Store front. Consists of 4 eq ops 1 plmbd not eq. Some Cap. Net $152K. # 4279.
OCEANSIDE - Leasehold & Some Equipment Only! Beautiful office in a single shopping center w/ 5 not eq ops in a 1,500 sqft ste. #4363
RAMONA (GP) - Established in 1979 and located in single strip mall. Busy area. Fee for service. Consists of 3 eq op. ID #4305.
SAN DIEGO (GP) - In free standing bldg w/ private prkng. Consists of 5 ops w/ Dentrix software. Monthly revenues of ~$40K. ID #4279.

VENTURA & SANTA BARBARA COUNTY

SANTA BARBARA (GP) - Well established practice w/ 3 eq ops in a 1,100 sqft ste. 100% Cash . Net $215K. Condo for sale. ID # 4393.

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How to Place a Free Classified Ad

The *Journal* has changed its classified advertising policy for CDA members to place free classified ads online and publish in the *Journal*. CDA members can place any classified ad. Non-CDA members can post employment classifieds or place display ads in the *Journal*.

All classified ads must submitted through cda.org/classifieds. Fill out the blank fields provided, including whether the ad is to appear online only or online and in the *Journal*. Click "post" to submit your ad in its final form. The ad will post immediately on cda.org and will remain for 90 days. Space permitting, your ad will run one time in the next issue of the Journal following the posting of your online ad. After 90 days, you will need to repost your ad if you wish to continue running it online. Note that CDA reserves the right to modify your classified ad for CDA style and to correct typographical errors.

Classified ads for publication in the *Journal* must be submitted by the fifth of every month, prior to the month of publication. Example: Jan. 5 at 9 a.m. is the deadline for the February issue of the *Journal*. If the fifth falls on a weekend or holiday, then the deadline will be 9 a.m. the following workday. After the deadline closes, classified ads for the *Journal* will not be accepted, altered or canceled. Deadlines are firm.

Classified advertisements categories are: Equipment for Sale, Offices for Sale, Offices for Rent or Lease, Available Positions, Opportunities Wanted and Practices for Sale.

How to Place a Display Ad

Nonmembers are welcome to place display ads. For information on display advertising, please contact Corey Gerhard at 916-554-5304 or corey.gerhard@cda.org.

CDA reserves the right to edit copy and does not assume liability for contents of classified advertising.

AVAILABLE POSITIONS

DENTAL ASSISTANT/RDA POSITION — Looking for full-time Dental Assistant/RDA position for a dental practice in Redwood City. Position available now. Candidate must be friendly, professional and a team player. Send your resumes to ddsbayarea@gmail.com.

DENTAL ASSISTANT — Our dental family if seeking a personable RDA with a minimum of three years of experience We are a family-oriented office who pride ourselves on providing the best dental care to each and every one of our patients. Our ideal candidate will be personable, warm, kind and friendly. Must be able to master the art of multitasking while maintaining a positive outlook even under stress. Our practice is an exquisite PPO insurance/fee-for-service, state-of-the-art facility where you would be proud to work. You would work Monday and Thursday with possible one to two Fridays or Saturday per month. Essential skills: excellent dental assisting skills; excellent knowledge of general and cosmetic dentistry (including digital X-rays, impressions, crown prep, whitening, treatment plans, note taking); knowledge of CEREX/E4D preferable; excellent communication skills; good attention to detail; friendly and personable disposition with the ability to interact professionally with patients and our team; experience with Dentrix practice

CONTINUES ON 846

WESTERN PRACTICE

800.641.4179
WPS@SUCCEED.NET
WESTERNPRACTICESALES.COM

BAY AREA

AG-194 SAN FRANCISCO: Established ~ 25 years. State-of-the-art equipment. Modern, spacious and spectacular office. Professionally designed and decorated with patient flow and office efficiency in mind! Richmond District off Land's End. 3,410 sf w/ 7 ops **$1.925m**

BC-175 EAST CONTRA COSTA: Vast employment, shopping & activities! 1,995 sf w/5ops **$300k**

BN-183 HAYWARD: ***Kick it up a notch by increasing the current very relaxed work schedule!*** 1,300 sf w/ 3 ops **$150k**

CC-151 SANTA ROSA: Stable patient base, well-respected, close to Memorial Hospital. 2,262 sf w/ 6 ops **$875k** *Real Estate avail.*

CC-170 SOLANO COUNTY: Minutes from nearby wine country! 950 sf w/3 ops **$225k**

CN-158 PETALUMA: Predominantly Capitation practice. 1,000 sf w/ 4 ops **Reduced! $395k**

CN-184 SOLANO COUNTY: Well established, premier practice. 2,180 sf w/ 5 ops. State of the art equipment **$775k**

CN-189 ANTIOCH VICINTY: In the heart of the beautiful California Delta! 3 ops **$275k**

D-9091 ATHERTON: Turnkey operation 969 sf & 3 ops ***Call for Details!***

DC-113 MILPITAS: Seller retiring! Great location 1,009 sf w/ 3 ops. Plumbed for 1 add'l **$110k**

DC-164 WATSONVILLE: Shopping complex/main thoroughfare. Modern & Attractive. 2,365 sf w/ 6 ops **$395k**

DG-116 SALINAS AREA: Large, loyal & stable. Popular Retail Center. 1,400 sf w/5 ops. State-of-the-art Equipment **Reduced! $195k**

DG-124 MILPITAS: Highly visible. Desirable area. 960 sf w/ 2 ops + 1 add'l **$130k**

DG-156 SAN JOSE: Hardwood Floors & plenty of windows! 1,160 sf w/ 3 ops (+2 add'l) **$145k**

DG-161 FREMONT: Beautiful office generating 40+ new pts/mo. 1,440 sf w/ 4 ops **$215k**

DN-204 SAN JOSE Facility: Located in a popular Dental Professional building! ~1,635 sf w/ 3 ops (+2 add'l) **$95k**

DG-202 SARATOGA Facility: Attractive, well-maintained, 2-story Medical/Dental/Professional building. Desirable upscale, affluent area. 1,568 sf w/ 4 ops **$185k**

BAY AREA CONTINUED

DC-191 MOUNTAIN VIEW: Rare opportunity! High quality, potentially large-scale practice. Heart of Silicon Valley. 2,000 sf w/7 ops (+1) **$950k**

DG-207 SUNNYVALE Facility: Location, location, location! Reasonable rent, low overhead, easy accessibility. 650 sf w/ 2 ops **$78k**

DG-212 FREMONT: One of the most beautiful practices we've listed! Courtyard Garden welcomes patients. Your talent and skill keeps them! 2,181 sf w/ 3 ops **$188k**

DG-214 CUPERTINO: **Seller highly motivated and will consider all reasonable offers! Opportunity to own property in the future. Highly desirable commercial corridor.** 1,200 sf w/ 3 ops +1 $100k obo

NORTHERN CALIFORNIA

EG-198 SACRAMENTO: Tucked in well established "Pocket Area" in highly desirable corridor. 1,112 sf w/3 ops **REDUCED! $140k**

EN-167 SACRAMENTO: One of the most desirable, affluent areas. 1,849 sf w/5 ops. **$450k**

EN-208 SACRAMENTO: Family-oriented FFS restorative practice! Office ~ 1,287 sf w/4 ops. **$225k**

FN-181 NORTH COAST: Well respected FFS GP. Stable patient base. 1,000 sf w/3 ops **SELLER MOTIVATED! $150k (25% int. in bldg. avail.)**

FN-087 LAKE COUNTY: Quality practice, friendly staff & Cerec 2,400 sf w/3+ ops **$699k**

FN-148 MENDOCINO CO: "Gateway to the Redwoods!" Quality care in 4 ops **$325k**

FN-185 UKIAH: Street-level office. 900 sf w/ 3 ops **$275k**

GN-134 REDDING: Stellar reputation, quality care and location! 2,264 sf w/4 ops. **$500k**

GN-149 YREKA: Quality FFS, Warm & Caring. 900 sf w/ 3 ops. Now Only:**$180k/Real Estate $110k**

GN-196 CHICO: Appealing location! ~2,510 sf w/4 ops **$150k**

GN-177 CHICO/OROVILLE: Spacious 2,500 sf w/6 ops **$399k**

GN-201 CHICO: Beautiful practice located on major thoroughfare with stellar reputation! 1,400 sf w/ 4 ops & room for another **$425k**

What separates *us* from other brokerage firms?

As dentists and business professionals, we understand the unique aspects of dental practice sales and offer more practical knowledge than any other brokerage firm. We bring a critical inside perspective to the table when dealing with buyers and sellers by understanding the different complexities, personalities, strengths and weaknesses of one practice over another.

Our extensive buyer database and unsurpassed exposure allows us to offer you…

A Better Candidate A Better Fit and A Better Price!

SALES

NORTHERN CALIFORNIA CONTINUED

HN-213 NORTH EAST CA: Close to the Oregon Broader, this FFS practice is ~2,200 sf w/ 3op +1 add'l **$145k**

HN-059 LASSEN CO: Quality, well-established, family-oriented. 1,600 sf w/3 ops **$120k**

CENTRAL VALLEY

I-9721 STOCKTON: Prof. complex. 1,450 sf w/ 3 ops & plumbed for 1 add'l **$75k**

IG-067 STOCKTON: Fully computerized, paperless, digitalized. 5,000 sf w/10 ops **Now $425k**

IG-165 TURLOCK: Well established Shared/Solo Group Practice. 10 ops (shared) **$428k**

IN-193 Modesto Facility: Recently remodeled! High foot traffic! Can be purchased with or without new equipment. 2,300 sf w/6 ops **Listed at only $224k**

IN-205 STOCKTON Facility: Get ready to practice your best dentistry here! One of the most desirable professional corridors. Newly remodeled. 1,565 sf w/ 4 ops **$169k**

JG-188 FRESNO: Loved, respected, Established! Net Profit over $350k! 1,452 sf w/4 ops **$390k**

JC-178 SAN JOAQUIN VALLEY: Historical Building in thriving area! 2,206 sf w/6 ops **$495k**

IN-211 MODESTO: Located in a single story, multi-unit Professional building, 1,500 sf w/ 4 ops. **$300k**

SPECIALTY PRACTICES

EG-131 ROSEVILLE/AUBURN Ortho: 2 practices within ½ hour of each other! **$175k**

I-7861 CENTRAL VALLEY Ortho: 2,000 sf, open bay w/ 8 chairs. Fee-for-Service. **$370k**

I-9461 CENTRAL VALLEY Ortho: 1,650 sf w/5 chairs/bays & plumbed for 2 add'l **$180k**

IC-163 CENTRAL VALLEY Perio: Well-respected FFS. 2,300 sf w/5 ops **$175k (Bldg: $250k)**

EN-203 SACRAMENTO Oral Surgery: This highly efficient office occupies ~ 3,000 sf w/ 4 fully equipped ops **$325k**

GN-209 SACRAMENTO VALLEY Endo: Be the one to carry on the stellar reputation and tradition! 1,400 sf w/ 3 ops **$350k**

ASK THE BROKER

I am buying a practice, but now my dentist friend says it is priced too high. What do I do?

Great Question. I firmly believe that only *YOU* can determine if it is priced too high. At first glance, that may sound ridiculous as you should have input from consultants and friends on this important decision, but let me explain.

PRICE

Price is generally a function of the local marketplace. A friend of mine recently purchased a 1,500 sq ft home for $1.1m after looking for more than a year. Someone from Kansas would think this is absurd. However, this house was in Marin County and truly might have been a great buy! The same holds true for dental practices. The price is usually dictated by the market. In an active market, this number usually falls into a "rule of thumb" range.

PRICE IS PROBABLY THE LEAST OF THE FACTORS THAT DETERMINES SUCCESS!

VALUE

The buyer's perception of value vs. price makes the practice either a good or poor decision for him/her. That value can ultimately only be determined by the individual buyer and is specific to that buyer. (Therefore generic PROJECTED incomes for the practice are worthless unless they are done for a specific buyer and his/her skill set). Of course, the buyer needs to do all the due diligence necessary to determine the value for his/her unique circumstances. The buyer also needs to understand exactly how the practice generates its revenues and determine how the practice might perform in their own hands. If they determine that they fall short on "filling the shoes of the older dentist", then they need a plan on how to deal with that. This could include working more hours, offering later appointments, signing up for more plans or a host of other ways to generate additional revenue. This is a long-term decision which needs to be addressed in a larger context.

IT'S NOT ABOUT THE PRICE - IT IS ABOUT THE OPPORTUNITY

I have seen practice transitions that were resounding successes even when priced well over 100% of gross receipts. In one particular case, the buyer's accountant and friends even advised her not to buy. However, she doubled the size of the practice in the first year! I have also seen practices fail that were practically given away and everybody thought it was a steal. So what's the difference? Your advisors and friends may not be aware of what kind of dentistry the Seller was doing. In addition to that, they may not know what type of dentistry you are capable of. You might hear of a dentist's horror story on a transition or a scratch start. In another dentist's hands, the result might have been totally the opposite.

CONCLUSION: **Price** will be dictated by the market. **Value** or opportunity is in the eyes of the beholder.

Timothy G. Giroux, DDS is currently the Owner & Broker at **Western Practice Sales** and a member of the nationally recognized dental organization, ADS Transitions.
You may contact ***Dr Giroux at*: wps@succeed.net or 800.641.4179**

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management software. The hourly wage will be competitive based on your experience. Please email your resume to Dr. Jamah at jamah@jamahdental.org.

ASSOCIATE DENTIST — We are state-of-the-art general offices looking for a good, board-certified specialist in endo, OS, perio. Requirements: U.S. graduates, teamwork, team leader, excellent communicator, well organized. Must bring your own specialty materials (endo rotary files). Compensation: 50 percent productivity (discussion will be in details). Locations: El Cerrito, Milpitas, Fremont, San Jose and Hayward. For El Cerrito, please email CV to richardlqh@gmail.com. For San Jose, please email CV to vunvhuy@yahoo.com.

ASSOCIATE DENTIST — Are you as passionate about dentistry as we are? Dentist sought for full-time/part-time associate/partner in hi-tech, hi-quality general/cosmetic/implant group practice. When it comes to technology, our office stands out: new Adec/Kavo operatories, Cerec 3-D Omnicam, iTero 3-D scanner, Galileos 3-D cone beam, digital X-rays, six different lasers including diode Nd Yag, WaterlaseMD, cold laser Zoom, Diagnodent, fully automated Control4 building, professional photographic studio with backdrops and strobes, Identafi oral cancer detection, patient massage chair, multiserver network, sterilization center, K-7 neuromuscular computer, tensing unit, air abrasion, rotary endodontics and high resolution pulse oximetry and the following dental specific software: Softdent, Consult-Pro, XCPT, Florida Probe, Venga intraoffice, Bite FX occlusion, Cross-Code. Dental Writer software and CEO. When it comes to cutting-edge services our office stands out: computer-guided implant surgery, neuromuscular dentistry, tissue engineering with (PRF,PRGF), airway management and sleep analysis, I.V. sedation, photographic smile analysis, Invisalign, PerioProtect, Sesame and

CAMBRA office. When it comes to research, publications and lectures we also shine: we have lectured, published or conducted clinical research with CAD/CAM implantology, porcelain veneers and cold laser therapy. We want the best. The best should have three-plus years of clinical experience with extensive documented post-grad C.E. to demonstrate your commitment as well as possible lectureship, research and or publications to your credit. Email resume to Heidi at Stratus Dental Management at hlevan@stratusdental.com.

DENTIST — We are looking for an experienced Dentist to work full time in our state-of-the-art practice in Salinas, Calif. This is a full-time position and our office is fully digital and equipped. We are only interviewing Dentists who have a minimum of four to five years of experience as a General Dentist and who can handle a busy schedule. This is a HYG practice. If you feel you are qualified, please email your resume/CV to jobs1556@yahoo.com. Excellent compensation.

DENTIST — Upland dental office is seeking a Periodontist/Implant Specialist to join our practice. We will need you one day, every other week. Please contact Elizabeth at 909.985.9866, fax resume to 909.931.0908 or send email to elizabeth@paulchangdental.com.

DENTIST — Kids Dental Kare is now hiring for the most in-demand area in health care: children's dentistry. The Affordable Care Act makes children's dentistry the ideal place for you to be if you have the skills and desire to help others. Minimum of three years experience is a must. Please send resume to HR@KidsDentalKare.com, visit us at www.kidsdentalkare.com. Location: Oxnard, Calif. Compensation: $500 base or percent of production (you determine your take home). Email resumes to dr.lanier@kidsdentalkare.com.

DENTIST — General Dentist needed in West Covina one to two days per week. Email resume to martinezj994@gmail.com.

ASSOCIATE DENTIST — Quality-driven, full-time Associate needed for a private, HMO-free practice located in Roseville, Calif. Must be an experienced General Dentist, motivated and proficient in all areas of C&B, endo and cosmetic dentistry. Office offers state-of-the-art equipment including Cerec and CAD/CAM technology. All candidates must have great chairside manner. Compensation is 30 percent of production. Please email your resume or CV to tonya@eurekadental.com or fax to 916.783.5393.

DENTIST — Our private dental office is seeking a part-time Oral Surgeon who can come in once a month for all of our oral surgery cases including implants. Office is equipped with 3-D CBCT, Nobel and Ankylos implant system. Interested applicants may fax their resumes to 510.245.3188 or email us at tdcoh@att.net.

ASSOCIATE DENTIST — Excellent opportunity for a Dentist who is willing to learn and grow with our practice in Chico, Calif. We are an established multispecialty practice with excellent supporting staff and patients. Must have good communicating skills and rapport with patients. Daily treatment schedules are mostly crown and bridge, bondings and exams. Other procedures include implants, removable partials and full dentures, which the other supporting GP can work on. Refer most endos and surgery out. Please email resume to gilbertlim@msn.com.

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DENTIST — We are seeking an experienced General Dentist for three to four days per week. Great opportunity to associate at our growing state-of-the-art private dental office. If you have at least four years of post-schooling experience and can provide quality dental care yet have consistently hit production goals, we invite you to email us your resume. Root canal treatment and extraction experience preferred. Implant and Invisalign experience a plus. All complex cases can be referred out to our in-house specialists. Please email your resume to bayareadentist2009@gmail.com.

TEAM LEADER FACULTY — Are you ready for a new opportunity? Have you considered using your clinical skills and knowledge to mentor the next generation of dental professionals? Western University of Health Sciences College of Dental Medicine in Pomona, Calif., is seeking Team Leaders to join our core of exceptional faculty and staff. The College of Dental Medicine is recruiting experienced, General Dentists or veteran team leaders to mentor students as they learn to provide quality patient care in a unique clinical learning model. The Team Leaders must be committed to providing a quality dental education within a university environment founded on the core values of humanism, caring, science and technical excellence. The Team Leaders will work in conjunction with each other and a Managing Partner faculty. The Team Leaders and Managing Partners are responsible for the operation and educational outcomes of vertical teams of students in a general dentistry, group practice model. The ideal Team Leader will oversee and demonstrate the ability to manage the full scope of general dental procedures offered in our comprehensive patient care model. The College of Dental Medicine has purposefully positioned the program as a premier center for integrative educational innovation, patient-centered interprofessional care and basic and translational research offered in a setting that utilizes advanced technology while promoting individual dignity and professional growth. The College plays a critical role in the unparalleled expansion that is advancing Western University of Health Sciences' status as a comprehensive health sciences and graduate university. WesternU has invested in the construction and equipping of two new state-of-the-art facilities designed to support program growth and development in an interprofessional environment. WesternU is located in beautiful Southern California. The area offers a warm climate with ready access to abundant outdoor recreation of all types. It is a short drive to ocean beaches, majestic mountains or desert landscapes. The area is home to renowned golf courses, vineyards and innumerable entertainment attractions for residents and visitors alike. To be considered for a position with the dynamic team at Western University of Health Sciences College of Dental Medicine, please submit a letter of interest and current CV to gmckenzie@westernu.edu. Western University of Health Sciences College of Dental Medicine 309 E. Second Street Pomona, CA 91766, www.westernu.edu.

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PRACTICE SALES • PARTNERSHIPS • MERGERS • VALUATIONS/APPRAISALS • ASSOCIATESHIPS • CONTINUING EDUCATION

ANAHEIM: General Dentistry Practice with 3 modern Ops. Gross receipts $423K with adj. net inc. $140K. Seller refers out specialty procedures. Retiring. Growth potential! #CA101

BAKERSFIELD: General Dentistry Practice. 3,650 sq. ft. suite with 8 Ops., 7 equipped. Digital X-rays and intra-oral camera. $1.2MM in collections. $453K Adj. Net Inc. Growing area. #CAM554

BAKERSFIELD and SMALL FARM COMMUNITY: Two Practices 30 min. apart. Strong patient bases. Staff and doctor work both. Underserved communities with room to grow. $588K gross. $278K adj. net. #CAM557

BISHOP: General Dentistry Practice & Building. 1,800 sq. ft., 5 Ops, '11 collections of $1MM. $387K Adj. Net Inc. #14390

CENTRAL COAST: Pedodontic practice with 4 Ops, Gross over $775K on 4-day wk. Great location. Over 800 new patients last yr. #CAM546

CENTRAL COAST: Prosthodontic practice with 4 Ops, full in-house lab. Over $1.1MM in gross receipts in '12. Near shopping. #CAM535

CERRITOS: General Dentistry Practice. 1,500 sq. ft. suite. 7 Ops, 6 fully equipped, 1 plumbed. Digital X-rays, SoftDent software. Near shopping, residential and freeway. 2012 adj. net $140K on $408K collections.. Room to grow. #CA100

CHICO: General Dentistry Practice. 2012 collections almost 1.4MM. 2,400 sq. ft. free-standing building. Option to purchase or lease. #14392 – In Escrow

COALINGA: General Dentistry Practice: 1,100 sq. ft., 3 ops, remodeled in '11. 1,000 active patients. Excellent opportunity for new dentist or dentist looking for satellite office. #CA564

COASTAL ORANGE COUNTY: General Dentistry/Implant Practice. 1,800 sq. ft., 4 Ops. Implant system in all Ops. Grossed $1.2MM in '11. #CA520

COASTAL ORANGE COUNTY: General Dentistry Practice. Retiring doctor spent $500K on 4 new Ops - high-end chairs, cabinetry and improvements. Dentrix and Dexis, Digital Pan. Near ocean - dream location! Gross Receipts $600+K in '11 and $500+K in '12. #CAM566

COASTAL ORANGE COUNTY: Periodontal Practice. 5 Ops. Retiring doctor works 3 days/wk. w/ 4 days of hygiene. '12 gross receipts $450K+. Great location near frwy./hosp. #CAM533

DANVILLE: FACILITY ONLY. 5 Fully equipped & furnished Ops. Digital X-ray, Digital Panoramic X-ray, and central Nitrous Oxide/Oxygen. Seller relocating. #CA548 – In Escrow

FOLSOM/EL DORADO HILLS: General Dentistry Practice. 1,200 sq. ft. 4 ops. '12 Gross Receipts of $405K., 2½ days hyg./wk. Dentrix, Laser, Digital X-rays, and Intra-oral cameras. #CA103

FREMONT: 3,000+ SQ. FT. SUITE, 10 Ops. Digital X-rays and Pan. 4,000 active patients. PPO/HMO with '12 gross receipts of $1.2MM w/ Adj. Net Inc. of $300K. #CA553

GRASS VALLEY: General Dentistry Practice. 1,500+ sq. ft. office. 5 Ops, 4 equipped. Collections of $491K. Adj. Net Inc. of $130K. #14379. – In Escrow

GRASS VALLEY: General Dentistry Practice. 2,000 sq. ft. condo. with 6 Ops. '12 gross receipts $442K. #14372. – In Escrow

GREATER CHICO/REDDING: General Dentistry Practice. 3 op office. Intra-oral, Pano, Imaging System, and Patient Education software. '12 Gross Receipts of $252K+. #CA104

GREATER SACRAMENTO: General Dentistry Practice. 1,400 sq. ft. with 5 Ops. '12 gross receipts $879K+, Adj. Net Inc. $446K. #CA525 – In Escrow

GREATER SACRAMENTO: General Dentistry Practice & Building. 2,300 sq. ft. with 6 Ops. EZ Dental Software, Pan, 8 days hyg./wk. $900K aver. prod. last 3 yrs. Great location. #CA560 – In Escrow

GREATER SACRAMENTO: Orthodontic Practice. Like-new 2,300 sq. ft. with extensive leasehold improvements. 6 chairs. 220 active patients phase 1. #CA551

HAWAII (MAUI): General Dentistry Practice. Approx. 1,200 sq. ft., 4 equipped Ops. Gross receipts $636K #20101

HOLLISTER: FACILITY ONLY: 1,800 sq. ft., 3 ops w/ 2 add'l plumbed with cabinets. Adec chairs, units, and lights, Dexis, Easy Dental, and Pano X-ray. Owner relocating to own bldg. #CA563

INDIAN WELLS: General Dentistry/TMJ Practice. 4,000 sq. ft. suite. 6 Ops. '11 Gross receipts $350K+ on 1 doctor-day/wk. #CAM530

LANCASTER: General Dentistry. 2,300+ sq. ft., 4 Op office. Gross receipts of $676K w/ $174K Adj. Net Inc. #14376

MILPITAS: General Dentistry. 1,440 sq. ft., prof. designed office in business district. 4 Ops w/ Intra-oral cameras and computers in each, plus Pano X-ray. Retiring. #CA562 – In Escrow

MURRIETA: General Dentistry. 1,300 sq. ft. with 4 Ops. '12 gross receipts $530K+ with $213K Adj. Net Inc. #CAM544

NEWPORT BEACH: General Dentistry. 4 Ops near Fashion Island. Dentrix, Gross Collections of $256K. Seller refers out most specialty work, room to grow. #CAM559.

NEWPORT BEACH: General Dentistry with 3 Ops, newer high-end equip., '12 gross receipts of $350K on 3 ½ days/wk. #CAM534 – In Escrow

NORTH OF SACRAMENTO: General Dentistry. Newly remodeled w/ 4 equipped Ops, 5 available. 1,500 active patients. '12 gross receipts of $515K on 32 hr/wk., 37 wks/yr. EZ Dental, Pan., Fiber Optics. 20 hrs. hyg./wk. Bldg. avail. for purchase. # CA558

NORTH OF SACRAMENTO: General Dentistry. 1,650 sq. ft. w/ 4 Ops. '12 gross receipts of $521K. Low OH 52%. #CA528.

NORTH ORANGE COUNTY: Endodontic Practice. 5 Ops fully equipped. 3 Zeiss wall-mounted microscopes. Gross receipts $370K and Adj. Net Inc. of $172K on 3 day wk. #CAM561

NORTH SAN DIEGO COUNTY: Large legacy practice. 12 equipped Ops. HMO practice with large CAP check-in, desirable area in North County. #CAM543.

ORANGE: General Dentistry. 5 Ops. 2012 gross receipts of $830K+. #CAM543 – In Escrow

ORANGE COUNTY: Periodontal Practice. 6 Ops, 5 fully equipped. '12 gross receipts of $450K on 4 day/wk. #CAM536

RIDGECREST: General Dentistry Practice and Building. 1,500+ sq. ft. building with 4 Ops. Small practice grossed $175K in '12. #CA523

SACRAMENTO: General Dentistry. 2,400 sq. ft. office/building with low OH (54%). 8 Ops, 7 equipped. '12 gross receipts of $642K #CA549 – In Escrow

SAN GABRIEL VALLEY: General Dentistry. 4 Ops. '11 gross receipts of $590K on 3 ½ day wk. #CAM541 – In Escrow

SAN JOSE: FACILITY ONLY 3,700 sq. ft. 6 ops. Digital X-ray, sterilization, computer workstations in every room. Reception w/flat screen TV, equipped business office and conf. room. #CA565

SAN JOSE: FACILITY ONLY Blossom Valley Prof. Location near Oakridge Mall. 1,200 sq. ft., 3 Ops, includes digital sensor, EagleSoft, and Computer Network. Move-in ready. #CA515

SAN JUAN CAPISTRANO: General Dentistry. 4 fully-equipped Ops. Gross receipts of $650K in '12. #CAM539 – In Escrow

SAN RAMON: FACILITY ONLY 1,400 SF with 4 Ops, equipped, 2 add'l plumbed, pano, computer server & workstations w/Dentrix, Intra-Oral Camera. Priced to sell. #CA511

SANTA CRUZ: Endodontic Practice. 850 sq. ft. office, 2 Ops w/ Schick Digital X-rays, Great satellite practice. Owner will work for buyer 1-1½ days/wk. Gross Receipts $350-$400K. 55% OH. #CA102

SOUTH ORANGE COUNTY: General Dentistry Practice with 5 Ops, 4 fully equipped. Specialty work referred out. '12 Adj. net inc of $324K on $739K collections. #CAM556

SOQUEL: General Dentistry in 1,100 sq. ft. office. 3 Ops in prof. bldg. near Hwy. 1. Gross receipts $338K on 2 day/wk. 2,200 active patients. 10 new/mo. Schick Digital X-ray, Dentrix software. Equip. 5 yrs. old. Moving. #CA550

TURLOCK: General Dentistry. Gross receipts in '12 over $950K w/ $443K Adj. Net Inc. #CA506 – In Escrow

WALNUT CREEK: Prosthodontic Practice with 3 equipped Ops and full lab. '12 gross receipts of $530K. #CAM540

YORBA LINDA: General Dentistry Practice with 5 Ops in great location. Laser, Intra-oral camera, and digital X-rays. 3 hygiene and 3 doctor days/wk. #CAM531

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CLASSIFIEDS, CONTINUED FROM 848

ASSOCIATE DENTIST — A great opportunity has become available for an Associate Dentist position. This is an opportunity to work in a very well established private dental office alongside an amazing staff. Part-time or full-time position available. We have a long-standing and loyal patient base. No HMO accepted. Ability to perform all facets of general dentistry including molar endo, extractions and cosmetic treatment required. New graduates welcome. Please email your resume to n_raiyani@hotmail.com.

FRONT DESK ADMIN — Our dental family if seeking a strong and personable front office team member. We are a family-oriented office with strong ethics and pride ourselves with providing the best dental care to each and every one of our patients. Our ideal candidate will be personable, warm, kind and friendly. Must be able to master the art of multitasking while maintaining a positive outlook even under stress. We desire the following from our future team member: Dentrix knowledgeable a must, G4 preferred; billing and collections and follow-ups; insurance and claim filing as well as follow-ups; treatment plan presentation; strong scheduling skills for both high production and hygiene; presentable, flexible, punctual, professional and detail oriented; experienced with Invisalign treatment presentation and billing; marketing, office promotions or incentives for new patient as well as tracking. To be considered for this position you must provide us with a cover letter, resume and references. We will provide competitive pay based on experience, and other exciting opportunities to the ideal candidate. Please email resume to jamah@jamahdental.org.

OFFICE STAFF — Amazing opportunity working in Dental Surgical Clinics. Exciting and rewarding. Great compensation potential. Must be dependable and willing to travel. Spanish a plus. phone 310.434.0040 or send email to aideeramirezrudolphortho@gmail.com.

OPPORTUNITY WANTED

ASSOCIATE DENTIST — Experienced and efficient female dentist looking for part-time/full-time Associate position in the greater Los Angeles area. High quality and service oriented, experience working in private practice setting focused on customer service. Proficient in all areas of general practice especially high-quality restorative and prosthetic dentistry including fixed, removable and implant assisted prosthesis. Licensed and experienced in pediatric oral sedation. Please email socaldds12@gmail.com for resume and other details.

EQUIPMENT FOR SALE

EQUIPMENT FOR SALE — New CEREC Acquisition Center. The CEREC Acquisition Center (AC) powered by Bluecam gives you access to a myriad of CAD/CAM restorative solutions that are every bit as reliable, proven and trusted as the company it comes from. Bluecam's LED technology takes digital impressions to the highest levels of precision and efficiency for impeccable results. CEREC AC provides you with access to the most comprehensive array of chairside CAD/CAM solutions; access to the highest level of digital impression precision and efficiency; access to connect with current and future digital dental technologies, processes and procedures Simply put, CEREC AC has the highest precision, ease of use and

CONTINUES ON 852

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4009 WOODLAND GP

Woodland GP and building available w/4 fully-equipped ops in approx. 1,500 sq. ft. office in gorgeous garden setting. Well est. prevention oriented family practice w/ seasoned & loyal staff. 2012 GR $232K+ w/just 3 doctor days. Only those interested in both the building and practice need respond. Practice asking price $138K, building asking price $315K.

3092 SF FACILITY

1,600 sq. ft. street-level dental facility in Marina/Cow Hollow neighborhood across from Presidio with excellent visibility and signage for foot traffic plus easy diagonal parking in front of building. Move in ready with 4 ops., 2 labs, kitchenette, reception and 2 desk areas plus 2 pvt. offices, 2 bathrooms, 1/2 basement & backyard with deck.

3096 NORTH BAY PERIO

Step into quality practice with established referral base. 2,200 sq. ft. office w/6 fully-equipped ops. Modern facility kept updated with recently purchased chairs, lights, Pano & lasers. Seller will grant a fair market lease and would consider selling the office space. 5 year avg. GR $1.2M+

3095 SAN CARLOS

Seller well-known for quality patient care retiring from established practice with loyal patient base, in highly desirable neighborhood. Asking $515K. SOLD

3098 SALINAS GP

Well-known GP specializing in restorative dentistry retiring from 28 year practice located in highly visible downtown office. 4 fully-equipped ops., Panorex, digital x-ray & recent equipment upgrades. 2 year avg. GR $331K+ w/approx. 152 doctor days/yr. Asking $210K.

3085 MODESTO GP

State-of-the-art practice in approx. 2,800 sq. ft. facility w/7 fully-equipped ops. This practice is for an established dentist or 2 dentists w/ experience & who will appreciate a high quality practice. Asking $745K.

4002 SANTA CRUZ AREA GP & BLDG

Well-est. practice in modern 1,250 sq. ft. office w/4 ops. 5 year avg. GR $630K+ w/ just 4 doctor days. Selling building & practice together. Practice asking price $430K, building to be determined. PENDING

4001 NORTHERN SONOMA COUNTY GP

Approx. 1,059 sq. ft. facility w/3 fully-equipped ops and dedicated parking in downtown area. Practice & building for sale. Great opportunity. Practice Asking $311K, building to be determined. SOLD

3094 NORTH BAY PERIO

North Bay Perio now available. Seller retiring from well-est. practice with seasoned staff and active referral base. 1,300 sq. ft. very nice office with 4 fully- equipped operatories. 2012 GR $450K+ with just 3 1/2 doctor days and 5 days of hygiene per week. Great upside potential since owner does few implants. Asking $271K.

4007 FREMONT PERIO

Seller retiring from 30 year est. Periodontal practice in 3 op facility located in medical/ dental building on well-traveled avenue in commercial neighborhood. Strictly Perio - no implants. Great starter practice opportunity, turnkey operation with equipment and no construction hassles. 2012 GR $133K+ w/just 1 Dr. day/week. Avg. 8 new pts. per month, 6 pts. per Dr. day & 7-8 pts. per hygiene day. Asking $75K.

3099 LOS GATOS GP

Well-est. general, restorative & cosmetic practice available in very desirable neighborhood. Gorgeous 1,530 sq. ft. office in single story dental complex w/4 ops. Asking $580K. SOLD

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CDA JOURNAL, VOL 41, Nº11

CLASSIFIEDS, CONTINUED FROM 850

speed than any system on the market today, whether for single units, full arches, or anything in between. Access CAD/CAM Superiority Bluecam Ease of use — simply position the Bluecam lens over the area to be acquired. Precision — the most advanced optical technology on the market yields precise 3-D models. Speed — shortest acquisition times for highly detailed images, including half-arch impression in 40 seconds and full-arch impressions in 2 minutes. Acquisition Center Battery pack — the convenience of moving from operatory to operatory without powering down. Small footprint — occupies minimal floor space, yet has a large 19" screen and a refined keyboard for optimal ergonomics and efficiency. Future-thinking platforms — access to CEREC Connect, the world's largest digital dental network, plus prepared for voice control and voice output. Ownership transfer from owner through Patterson — only did 10 crowns — so everything is brand new. Call my cell phone 408.667.5566.

EQUIPMENT FOR SALE — Global Urban Ceiling-Mounted Dental Microscopes. I have two scopes with optics and halogen lighting. Both have complete ceiling mount system. I have an additional unused ceiling mount which I will include. These scopes are approximately 13-15 years old. Asking $12,000. Call 909.496.1009.

OFFICES FOR RENT/LEASE

OFFICES FOR RENT/LEASE — Dental office space, 2,500 sq. feet on 40th St. and Waterman Ave. in San Bernardino available for rent. Excellent for orthodontist, prosthodontist or any specialist to start or relocate practice to San Bernardino. Four operatories ready to use with lab space, lunchroom, consultation room and beautiful courtyard. Please call 951.536.8419 for more info.

OFFICES FOR RENT/LEASE — Specialty office in Bakersfield, Calif., for rent/lease. Newly remodeled, 1,000 sq. ft. established dental office with four plumbed operatories. Quiet room. Tremendous amount of under serviced young families in the area. Perfect for pediatric dentist, endodontist or oral surgeon. $1,250 a month. Please call 661.871.0780.

OFFICES FOR RENT/LEASE — Wilshire/Brentwood/West Los Angeles — New GP office space to share. Great location with parking. Principle practices part-time. Perfect for start-up, existing or retiring practice. Flexible terms and availability. 310.478.3511.

OFFICES FOR RENT/LEASE — Office space available. 2,700 sq. ft. on ground floor, easy access, good visibility, excellent parking. Will remodel to suit. 510.384.5553.

PRACTICES FOR SALE

PRACTICE FOR SALE — Practice for sale in Ventura, dentist is retiring. Office has four operatories and is about 1,600 sq. ft. Current rent is about $1,300 per month. Phone Dr. John Seo at 805-676-1800 or 805-512-3311.

CONTINUES ON 854

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RARE OPPORTUNITY - SAN FRANCISCO'S EAST BAY - VERY TRENDY LOCATION
2012 collected $1.9 Million. 2013 trending $2.2+ Million with Available Profits of $1.3 Million.

Performance realized by One Dentist. Surprisingly, this practice is not close to realizing its potential. Smart Successor who tweaks the practice where it needs to be tweaked shall then make this into something special. Paperless and digital. Ambitious SoCal Dentist who is not averse to commuting should consider this opportunity. Location shall be constant New Patient generator. Great Two Dentist purchase. Make this a "One Stop" Shop. Little competition with phenomenal upside.

Full Price $1.2 Million. Contact Ray Irving at 415-899-8580 or Ray@PPSsellsDDS.com.

6053 SAN FRANCISCO'S SOUTH BAY – PEDO PRACTICE Long established. 2013 tracking $660,000 in production, $650,000 in collections and $255,000 in Available Profits. Great staff.

6052 BERKELEY Trendy north side shopping area. Very strong foundation. 2,000 active patients. 4-days of Hygiene. Beautiful hitech office with great curb appeal. 2012 collected $590,000. Lots of work referred out. SOLD

6050 MERCED 2013 trending $360,000. Very profitable. Refers Endo, OS & Perio. Not a Delta Premiere Practice. Great foundation to build upon. Full Price $125,000.

6048 SALINAS Great opportunity for the ambitious, Ideal for two Dentists. 10 days of Hygiene per week. 2012 collected $1.1 Million. 2013 tracking $1.2 Million. Practice did well during Great Recession.

6047 STOCKTON Best location outside Brookside Community on West March Lane. Annualized revenues of $540,000. Attractive 3-Op office. Package sale includes condo.

6046 PINOLE Collected $500,000 in 2012. 4-days of Hygiene produced $178,600. Beautiful office. Refers Endo. Lots of Goodwill here.

6045 MANTECA / MODESTO AREA'S RIPON Great location. 3 Ops, 2 more wired & plumbed. $180,000 invested here. Practice did more when Owner worked harder. 2012 collected $327,000 on 3- day week with 5-weeks off.

6044 MODESTO Best location. New development occurring nearby. Collects $380,000. Digital x-ray computers in Ops. Very attractive office. SOLD

6043 EL SOBRANTE 3-day practice collected $170,000 in 2012. 3-Ops. Building optional purchase.

6041 PLEASANT HILL Collected $365,000 with Profits of $142,000 in 2012. Owner slowing down. Previous 3-years averaged collections of $415,000 and Profits of $180,000.

6039 CALIFORNIA'S SOUTH LAKE TAHOE. Long established. 2012 collected $515,000 with 3 months off. Realized Profits of $230,000+. Attractive 3-Op office. SOLD

6008 MENDOCINO COAST'S FORT BRAGG Cultural haven offers attractive lifestyle. 2012 collected $750,000. 2013 shall top $800,000. 4-days of Hygiene. Digital radiography. Computers in Ops. Full price $235,000.

TEMECULA - MURIETTA VALLEY Hi identity. Classic GP. Gorgeous 6-Op office. Grosses apprx $800K. Right Buyer can gross to $2 Million in 5-years. Valuable Dental/Professional Building also available.

PASADENA AREA $6K-to-$7K/mth in HMO. Grossing $750,000 part-time. Did $1+ Million when Owner spent more time here. Full Price $850,000.

FONTANA 100,000 autos pass daily. Hispanic. PT Owner grosses $250K. FT Successor should Gross $500K+. Remodeled. Firm price $275,000.

ALISO VIEJO Best Shopping Ctr location. Grosses almost $1 Million. 5 ops "state-of-the-art". PT Owner. Wants "hands-on" Owner. Work here, live at beach! Over 70 NPs/month. FP $900,000.

CUCAMONGA 50 NPs/mth. Located off freeway exit. 5-ops. Beautiful Grossed $850K in 2012. Should do $1.2 in 2013. FP $850,000.

RIVERSIDE Hi Identity building 4 Sale. Elegant 5-ops. CT digital Pan & x-rays. PT Conservative Female Owner Grossed $550K. One PPO. Full-time Successor shall do better.

RIVERSIDE Grosses $1.3 Million. $6-to-$7K/mth from HMO. Does ortho. 10-ops in 3,000 sq.ft. with low rent. Hi identity Shopping Ctr near Wal-Mart. FP $1 Million.

IRVINE Grossed $1.2 Million in 2012. 2013 should do $1.3+. 5-ops. Absentee Owner. Unique transition assistance available. FP $1 Million.

SAN FERNANDO VALLEY Best location. Grosses $1.2 Million. Lots of work referred. This is $2 Million location. 8-ops. 30 Hygiene pts/ day. Full price $1.2 Million.

SAN FERNANDO VALLEY – BEST HISPANIC LOCATION 7 state-of-art Ops, room to expand. 70 NP's/mth. Building part of sale. Another $2 Million location.

TORRANCE – GARDENA Very conservative Chinese DDS. Lots of work referred. Young Chinese/AM Successor will do $600K. FP $185,000.

LANCASTER Established location. Equipped. Seller needed more room. Many walk-ins each day. Seller did $900,000 here. FP $125,000.

BALDWIN PARK 80% Hispanic. High identity building. 3-ops. Grosses $250,000. FP $150,000.

BAKERSFIELD Grosses $750,000. Established 50-years. 5-ops. Successor should do $1 Million. FP $500,000.

SMALL TOWN NEAR BAKERSFIELD Practice & RE. Gross $400,000 with full time DDS. Practice & Building $350,000.

ORANGE Female DDS doing $30-to-$40K/mth part-time. Seller will work-back for smooth transfer. FP $295,000.

VICTOR VALLEY High Identity Shopping Center. Grosses $650,000. 8-ops, low overhead. FP $550,000.

REDLANDS Low overhead, 5-ops, digital. Gross $30,000+/mth. FP $350,000.

NEVADA Small resort city near Las Vegas. 5 state-of-art Ops. Grosses $600K 3-days. Will do $600K more with 3 more days. FP $600,000.

DENTURE CENTER 30+ denture patients/day. Grosses $1.3 Million. Patients ask "Will you do Implants?" Answer always "We just do dentures." Specialist will take to $2 Million. FP $1 Million.

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CLASSIFIEDS, CONTINUED FROM 852

D&M

PRACTICE SALES AND LEASING

Paul Maimone
Broker/Owner

HAPPY THANKSGIVING

BAKERSFIELD #26 – 3,500 sq ft free stand. duplex bldg. w a (5) op fully equipped turnkey dental office. Located on a main thoroughfare w monument signage. Move in condition.

BAKERSFIELD #27 – (4) op comput G.P. starter pract. 2 ops of new eqt. (2) add. plmbd ops. Opened June 2012. (12) mos Gross Collect $75K p.t. & growing. Mixed pts. Seller moving. ***NEW***

BEVERLY HILLS – Great startup or second office. (2) op Turnkey Office. Leaseholds & eqt'd. No charts. Located in a smaller two story prof. bldg. on a main thoroughfare. Low rent. ***NEW***

CENTRAL VALLEY/So. FRESNO COUNTY – (3) op comput. G.P. in smaller town w ltd. competition. Newer eqt. Networked & digital. Dentrix & Dexis. Gross Collect $40K+/mos.

CORONA – Dental Spa & Free Stand. Bldg. for sale. (5) op comput. G.P. w (2) spa rooms; one for facials & one for massage. Drop dead gorgeous facility w all the special touches. New eqt. Digital x-rays. Pano eqt'd. Production of $1.0M+ on a (4) day week.

EAST VENTURA COUNTY – (3) op compt. G.P. Fee for Service. Located in a smaller prof. bldg. w some exposure & visibility. Pano eqt'd. 2013 Proj. Gross Collect $500K. ***SOLD***

ENCINO – (4) op compt G.P. in a well-known, recently remodeled prof bldg. on a main thoroughfare. Magnificent panoramic Valley views in (3) ops. Cash/Ins/PPO. Gross Collect $600K/yr on a (4) day week. Digital X-Rays & laser eqt'd. 34+ yrs of GoodwilL. ***PENDING***

HAWTHORNE – (7) op compt. G.P. in a free stand. bldg. on a main St. Exposure & visibility. (6) ops fully eqt'd. Digital X-rays. Cash/Ins/PPO. Many walk-ins. Collecting $30K+/mos. ***NEW***

OXNARD #7 – (5) op turnkey G.P. No pts. In a free stand bldg. on a main thoroughfare.

SAN JOAQUIN VALLEY – G.P. & Bldg. in small town w ltd. competition. (4) op comput. office. Cash/Ins/PPO. Annual Gross Collect $500K+. Low overhead. Seller retiring. ***REDUCED***

SANTA CLARITA VALLEY – Cash/Ins/PPO bread and butter practice. (4) ops eqt'd. Located in a medical/dental/professional bldg. complex. 40+ yrs of Goodwill. Seller retiring. ***NEW***

WEST SAN FERNANDO VALLEY PEDO/ORTHO OFFICE – Comput. Pedo/Ortho office. (3) op open bay & (1) op quiet room. Pano eqt'd. Digital X-rays. Cash/Ins/PPO small % Denti-Cal. 30+ years of Goodwill. Annual Gross Collect $600K+. Seller retiring but will assist with transition and/or stay to do Ortho.

WOODLAND HILLS #4 – Beautiful state of the art (9) op comput G.P. in a Shop Ctr. on a main thoroughfare. Excellent exposure/visibility/signage! (6) ops eqt'd w newer eqt. (3) add. plumbed. 2013 Projected Gross Collect $370K on a 3-3.5 day wk. Cash/Ins/PPO/HMO pts. ***SOLD***

UPCOMING PRACTICES: Agoura, Alhambra, Beverly Hills, Camarillo, Covina, Glendora, Montebello, Monrovia, Pasadena, SFV, Torrance, Ventura, West Covina, & Westchester.

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PRACTICE FOR SALE — Energetic, healthy 70-year-old Dentist who has practiced for 40 years in Clairemont Mesa neighborhood of San Diego wants to start an exit plan in four years. You can develop your own practice in the four operatories while I taper and take more time off. The practice has never been marketed. I work only three days. Another dentist practiced in this office for the last 14 years but recently died. Attractive terms as you gradually buy my practice. hrblock@san.rr.com. Call 619.892.0931 for more information.

PRACTICE FOR SALE — Dental office for sale in Bakersfield. Located near Spanish supermarket. Heavy traffic. Five operatories (approximately 1,600 sq. ft.) Monthly rent (including triple net): $2,500. Patients population: 5,000. Office has been qualified for EHUR funding from the feds. You still could get that fund if you apply (max. $60,000). I have been working part-time (20 hours per week) at this office for seven years. Gross income: $200,000. Asking: $135,000 Please don't contact my office. If you have any question, please call my cell phone 661.932.3817.

OPPORTUNITIES WANTED

OFFICES FOR RENT/LEASE — I'm looking for a dental office for sale or a dental office space for lease in the areas of Ventura County, Victorville, Lancaster or Central Valley, Calif. Please reply to ddscalifornia9@gmail.com.

LA PRÁCTICA DENTAL EN VENTA — Dentista Hispano compra directamente practica dental acreditada en una de las siguientes areas: Santa Ana, Anaheim, Long Beach, Riverside o Bakersfield. Preferiblemente vendedor ayude en la transicion. escribir al correo luismiguelcollazos@yahoo.com.

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6. Lease negotiations.

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ADVERTISER INDEX

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CONTINUED FROM 858

where in a class of 125 students, I was designated as "76." I assumed this listing was in order of aptitude and was pleased that 49 other students were judged dumber than I was. Four years later, the graduating class numbered 85 and I was ***still*** number 76. I felt the attrition rate was entirely due to loss of self-esteem by the three-digit group that became disoriented during the daily roll call and dropped out, but it was obvious that had the curriculum extended another two years, I would have emerged the dumbest, hands down.

I could see where this was going and I was correct. I had a problem with the number 55. A few years ago, it was the federally mandated speed limit, so all the fast people had to slow down. Now I live in a place where the residents have decelerated dramatically to the speed of bingo, but are required to be beyond 55 to qualify for a place to lay their heads.

Long before I reached senility — a pursuit still in progress — my life was flooded with numbers. Worse yet, I was not allowed to choose these numbers. My favorites, 9 and 11, were not available and I was forced to memorize all sorts of combinations and permutations. Every facet of my existence was assigned a number by some faceless nonentity who carelessly assigned numbers like 8 and 4 that were hard to write or erase. Even my typewriter couldn't tell the difference when faced with 1, l or I.

Today, to have anything sent to me, talk to an authority, gain entrance into my computer or any of its millions of password-required sites, I have to give up a number, different from every other human being's. Telephone, driver's license, street address, height, weight, how many times I have to get up at night, medical prescriptions, credit cards, accounts — everything has indelibly recorded a number for me, all different.

Let's start with the DMV. I know the DMV is a poster boy for all manner of complaints, not the least of which is when the number you're issued is contaminated with a letter. My letter is Z followed by another letter, O, except it ***isn't an O!*** It's an O with a red diagonal line through it. That makes it a zero, or another O or a zip, nada, zed, zilch or a nothing. Letters and numbers should never appear together in the same group.

When a child outgrows his first number such as "fwee sebenty eleven fo," he will be allowed a one-time choice of an alternative number with no spell-checker requirement.

Now pay attention, this is the crux of my idea: you will notice that all these various number entities labeled as ***your*** number is ***not*** your number, it is theirs.

These numbers have no meaning to you other than trouble. A credit card typically has 16 numbers on it, with another four to warn you that it has expired. Throw in three more on the reverse side for "security reasons." Twenty-three numbers!

These numbers are so astronomically high that words like "gazillion" and "ginormous" had to be invented. Of course, we know that these large numbers are just a bunch of little numbers all joined together so they can be translated to reveal more about your affairs than anybody has a need to know, which brings me to my point, I think. My point is, you can't remember all the various numbers; they are too long, meaningless to you and are assigned by strangers you would instinctively dislike if you knew them. It's like tracking the scoring of cricket, a complete waste of time.

My plan: Starting about the time a child is able to hold up four fingers when asked how old he is, he will get to pick his own personal number. Avoid 13, this is a "bad" number; try 7 or maybe 21. This will remain with you for the rest of your life. The bank has it, the computer has it, SoCal Edison and the DMV have it. A mortician will get it. One exception — every government agency except Social Security should have it. You don't want to hazard an account change with SS. It is going to ***send*** you money, unlike all the others that want the reverse.

My self-assigned number will be 11281947. The significance of that sequence is simply Nov. 28, 1947. If there is a conflict with some other person married on that same day, I'll just add 1428. What are the odds that his ceremony took place at 4:28 p.m., same as mine?

Married and divorced people should have no trouble remembering their numbers. Multi-divorced parties should choose the "stop speaking" date that eventually cost them the most money. When a child outgrows his first number such as "fwee sebenty eleven fo," he will be allowed a one-time choice of an alternative number with no spell-checker requirement.

If you have any questions about this proposal, contact The National Bureau of Statistics, Washington, D.C., at 1+202.755.1212, ext. 4783695241. Ask for No. 93874462299947Z0. That's Phoebe, she speaks numbers. ■■■■

We're Taking Your Requests

If you have a favorite Dr. Bob column you want to see again, send an email to Publications Specialist Andrea LaMattina at andrea.lamattina@cda.org. We will oblige by reprinting those requested favorites interspersed with any new Dr. Bob submissions.

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The Numbers Game

My favorites, 9 and 11, were not available and I was forced to memorize all sorts of combinations and permutations.

Robert E. Horseman, DDS

ILLUSTRATION BY VAL B. MINA

The world's gone mad, completely bonkers. Angry readers of newspapers, protestors and antiprotestors of every stripe, marching with righteous indignation, waving banners, signs, muttering or yelling at their TVs. If you haven't joined them, you simply don't know what's going on. We all agree on that; lots of frothing disagreement over why, when and what to do about it. The winter of our discontent has become an all-season annoyance.

I know how it started — at least with me — and I'm working on a plan to zero it down. The problem is ***numbers.*** It shouldn't be such a problem; there are just 10 of them, zero through nine, although some nitpickers claim O isn't a number. Yes, it is.

"What did you get on your exam?"

"O."

"So, it's a number."

"No, it isn't. O is nothing."

"Wrong. If that were true, even people who didn't take the exam would get O. That would lead to a lot of confusion."

"I see your point."

After I more or less mastered the multiplication tables, I thought I was through with numbers as evidenced by my unsuccessful jousting with algebra and trigonometry. At least the grading was alphabetical where a D in a straight line was more understandable than a 62 based on a curve.

I lost my alphabetical identity to a numerical one later in dental school,

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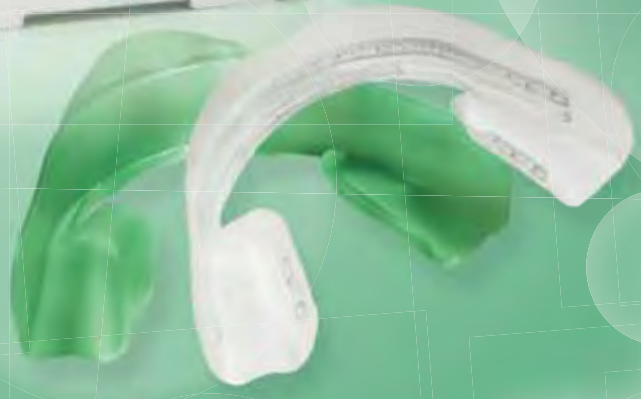

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