Clinical Relevance and Potential Utility of Diagnostic Tests

Philippe P. Hujoel

Department of Dental Public Health Sciences and Department of Epidemiology, School of Dentistry, University of Washington, Seattle, USA

Summary: Since the 1970s, diagnostic tests have been evaluated using a hierarchical six-level framework. Within this framework, clinical relevance and potential utility represent level 4 and 5 evidence and is typically assessed by means of randomized controlled trials where diagnostic tests are randomized and the decisions made by clinicians (level 4 evidence) or the tangible outcomes observed in patients (level 5 evidence) are tabulated. Using such an evidence-based framework within dentistry would be particularly useful for assessing diagnostic tests aimed at detecting subtle changes or involving ionizing radiation. Diagnosing subtle anatomical, crevicular fluid, or microbiological changes in the oral cavity of symptom-free patients has the potential to drastically increase dental disease prevalence and dental treatment utilization. Experiences with diagnostic tests in other disease areas such as prostate cancer indicates that such redefining of disease leads to uncertainties in assessing harm-benefit ratios because it often is unclear whether those subtle changes that can be detected and treated need to be treated, and whether those subtle changes that need to be treated, can be detected and treated. Diagnostic tests involving ionizing radiation can have potentially adverse health consequences, and additional pressures exist to provide evidence that their benefits outweigh harms. Considering the high prevalence of radiation usage and the lack of individual-patient dose-monitoring, there is a need to determine which radiographs improve patient outcomes. The high potential impact of dental diagnostic testing on dental utilization combined with the high prevalence of dental visits make it that an evidence-based framework of the assessment of diagnostic tests would offer a welcome addition to the dental knowledge database.

Key words: diagnostic testing, patient benefits, ionizing radiation, harms


INTRODUCTION

The methodology for assessing the value of diagnostic tests was largely established in the 1970s and has now been widely adopted by evidence-based treatment centres and the Agency for Health Care Research and Quality Assessment Technology Program (Thornbury et al, 1975; McNeil and Adelstein, 1976; Fineberg et al, 1977; Fryback, 1983; Tatsioni et al, 2005). The methodology consists of a six-level hierarchical framework with the lowest level being the technical feasibility of the diagnostic technology and the optimization of its usage (level 1) and the highest level being the societal impact of diagnostic testing (level 6) (Table 1). Most relevant to this report, assessing the clinical relevance and potential utility of diagnostic tests, is determining how diagnostic testing impacts on treatment decisions (level 4 evidence) and more importantly, how diagnostic testing provides tangible patient benefits in terms of how a patient feels, functions, or survives (level 5 evidence).

The clinical utility of dental diagnostic tests varies widely. For instance, correct imaging of the inferior alveolar nerve (IAN) vis-a-vis the implant body is of such importance in avoiding IAN damage that even a suggestion of randomizing patients to have access (or not to have access) to radiographic techniques for IAN visualization would be unethical (Worthington, 2004). On the other extreme, the use of a cephalographic radiograph to document the end of orthodontic therapy is of such dubious clinical utility that spending resources on a formal evidence-based assessment of the value of such practices appears to be a waste of resources. Between such extremes, there are those dental diagnostic tests where it remains unclear and controversial whether diagnostics testing leads to tangible patient benefits and where a formal assessment of diagnostic test value would be most productive.
Two areas of diagnostic testing have the potential to have a significant impact on the profession of dentistry and will be discussed further. First, there are those diagnostic tests aimed at detecting subtle changes in the oral cavity. Enamel de- and re-mineralizations, subtle bone-remodelling processes as a potential sign of periodontitis, or biochemical or microbiological markers of inflammation have the potential to drastically increase dental ‘disease’ prevalence and are increasingly used to advocate for early intervention. An evidence-based assessment of the utility of such diagnostic tests is overdue. Second, there are those diagnostic tests that may be harmful in and of themselves. Ionizing radiation is the most prominent member of this class of diagnostic tests and, with certain countries reporting that over 50% of the population is exposed to dental radiation, there is a need to provide an evidence-based assessment of the benefits.

**Diagnostic Tests Aimed at Detecting Subtle Changes**

Substantial resources have been spent in dental research on the development of diagnostic tests aimed at detecting subtle changes. Examples include those diagnostic tests aimed at detecting bacterial or host enzymatic activity in gingival crevicular fluid, methods aimed at detecting subtle enamel demineralizations, microbiological testing for a cariogenic bacterial challenge or purported periodontal pathogens, and differential dark field microscopy. Their success in terms of adoption in clinical practice has varied widely.

For many of these diagnostic tests, the clinical relevance of what is being detected is not completely understood and epidemiological evidence relating the subtle changes to clinically relevant outcomes is often lacking. For instance, the role of bacteria in the periodontitis process (not gingivitis) continues to be an often-changing and increasingly complex story that remains to a large extent unsupported by epidemiological evidence of causality. Developing diagnostic tests aimed at detecting these bacteria has a long scientific road ahead to establish clinical utility. Similarly, the benefits of detecting early enamel lesions rest on biological plausibility, not epidemiological evidence. Small clinical studies suggest that most enamel demineralizations may not progress (Backer Dirks, 1966), that many frank cavities are observed without observing a preceding white spot (Katz et al, 2005), and that ‘bad’ remineralizations (hidden cavities) may occur (Koulourides and Cameron, 1980). Treatments effective on preventing subtle enamel lesions may not be effective in preventing frank cavitations (Zimmer et al, 2001). Consequently, diagnostic tests aimed at detecting subtle enamel demineralizations have unclear clinical significance. For many chronic diseases, possibly including cancer, periodontitis and oral cancer, the important question is whether those subtle changes that can be reversed need to be reversed, and whether those subtle changes that need to be reversed can be reversed. Making diagnostic tests aimed at detecting subtle oral changes in otherwise healthy patients without answers to such questions make it possible to drastically increase treatment utilization, cost, and potentially harm to the patient, without materially changing the clinically relevant dental disease outcomes.

Dental diagnostic tests aimed at detecting subtle changes should be based on level 5 evidence (Table 1) - the conduct of randomized controlled trials where patients are randomly assigned either to access or no access to diagnostic tests and where the clinically relevant outcomes in both groups are compared. Diagnostic tests such as prostate-specific antigen (PSA) testing are currently being evaluated using such an approach (Schroder, 2005). Hopefully, diagnostic testing for chronic dental diseases will follow such examples and provide the same type of reliable evidence that is available for medical diagnostic tests.

**Diagnostic Tests That Involve Ionizing Radiation**

While the radiation doses with dental radiography are typically considered to be very low, there is a concern regarding potential adverse health effects. Some suggest that the lowest dose for which good epidemiological evidence exists of an increased cancer risk with an acute exposure is 10 to 50 millisievert. This dose is higher than most typical dental radiographic exposures (Brenner et al, 2003). Cumulative dental radiography doses can cross this threshold and can be of concern since some of the most radiosensitive organs in the body, the thyroid and the meninges, can be in the direct field of the radiation beam. Several studies have raised concerns that dental radiography may be associated with intracranial meningiomas (Preston-Martin et al, 1980, 1983, 1989; Rodvall et al, 1998; Longstreth et al, 2004), thyroid cancers (Hallquist et al, 1994; Wingren et al, 1997), salivary gland tumors (Horn-Ross et al, 1997) and adverse reproductive outcomes (Goldberg et al, 1998; Hujoel et al, 2004; De Santis et al, 2005).

Studies showing such associations typically have little impact on diagnostic practices in dentistry both because the results are often at odds with interpolations of the atomic blast experiments, and because radiation doses have been continuously decreasing. These two reasons combined with advocacy of the ALARA principle (as low as reasonably achievable) have left diagnostic X-ray practices under-evaluated over the past 40 years.
The ALARA-principle however is toothless. In the absence of evidence-based assessments of clinical utility, both the orthodontist who requests, in addition to the standard orthodontic series, a CT-scan of the mandibular joints for every patient with a midline discrepancy, and the orthodontist who only request a panoramic radiograph to determine missing teeth can be said to practice according to the ALARA principle. Yet the radiation doses to radiosensitive organs can differ by magnitudes as much as 100. With lack of knowledge regarding radiation doses common, and the absence of a reliable cumulative patient record of lifetime received radiation doses, there is little or no control over a person’s total lifetime exposure to dental radiography.

The recent National Academy of Sciences report (Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation NRC, 2005) that there is no such thing as a safe radiation dose emphasizes the need to develop evidence-based guidelines, not opinion-based guidelines as to which practices involving ionizing radiation provide unequivocal tangible patient benefit. Higher levels of evidence (e.g., randomized trials) on the value of X-rays in many dental specialties have the potential to provide a firm scientific footing as to which, if any, radiographic practices indeed provide tangible patient benefits in terms of treatment outcomes. Such studies would provide the opportunity to determine what visualization techniques for which procedures/interventions/monitoring do impact on the ultimate outcome that the patient perceives.

## CONCLUSIONS

The primary goal of a diagnostic test is to improve patient clinical outcomes. While it is often assumed, based on biological plausibility, that most dental diagnostic tests achieve this goal, direct evidence in support of this is often lacking. Given that the current diagnostic tests of interest have the potential to drastically increase dental disease prevalence, and given that diagnostic tests that involve radiation will do harm on a population-level, and given the world-wide high utilization of dental diagnostic tests, the adoption of the six-level framework for assessing and evaluating dental diagnostic tests could be a welcome addition to the dental knowledge database.

## REFERENCES


Reprint requests:
Philippe P. Hujoel, D.D.S., Ph.D.
Department of Dental Public Health Sciences
School of Dentistry
Box 357475
University of Washington
Seattle, WA 98195
USA
E-mail: hujoel@u.washington.edu