1
2001

Inspektor Research Systems bv
Quellijnstraat 92
NL - 1072 XX Amsterdam
Tel. +31 - (0)20 - 67 64 988
inspektor@inspektor.nl

news letter

Inspektor Research Systems bv

Contents

New products launched by Inspektor

This summer, Inspektor launches two new products for fundamental caries research: QLF-InVitro and TMR-2000. Both products are expected to have significant impact on current research.

QLF-InVitro

Click picture

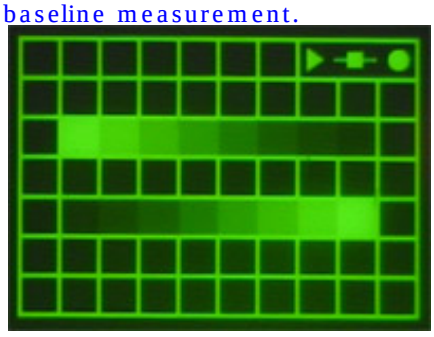
Inspektor proudly announces the launch of QLF-InVitro: a new tool for fundamental, quantitative caries research.
QLF-InVitro will revolutionize research by the ease, the speed and the effectiveness it will bring to de- and remineralization studies.
QLF-InVitro is based on Inspektor's patented Quantitative Light-induced Fluorescence (QLF) technology that uses visible light to detect incipient caries.

QLF-InVitro advantages

The purpose of QLF-InVitro is to measure changes in mineralization of tooth-tissue in a nondestructive way. Tooth-tissue specimens that are used in in-vitro or in-situ experiments can be measured repeatedly without the need to cut the specimens as is the case with Transversal Microradiography (TMR), Longitudinal Microradiography (LMR), Polarized Light Microscopy or Histology. Because of this nondestructive approach, in-vitro and in-situ experiments can be designed around smaller amounts of specimens without loss of analysis power. Also, the time needed to measure the specimens is reduced dramatically, typically from days to seconds. No more X-rays, no more film development problems: just take your specimen, measure it and replace it in the test environment.

QLF-InVitro results

De- and remineralization is measured in terms of the change in fluorescence (ΔF) over an area (A), which is referred to as ΔQ ($=\Delta F \cdot A$). Optionally, ΔQ values can be converted into Integrated Mineral Loss (IML) values as used by TMR and LMR. Typically, ΔQ will be measured longitudinally with respect to a baseline measurement.



QLF-InVitro results are reproducible by using a special calibration specimen with known grayscales. The calibration process, which is fully supported by the software, is part of the installation and ensures that measurements of QLF-InVitro are reproducible and allows comparison of results between different QLF-InVitro systems as well as different video cameras.

Focus on: Inspektor newsletters

This is the first Inspektor newsletter. With the approaching introduction of QLF (Quantitative Light-induced Fluorescence) for clinical practice, we felt that it was time to create new ways to inform the field about the potential and the progress of Inspektor's development.

QLF-InVitro equipment

The equipment consists of the specimen stage and the system box. The system box (30.6 x 33.8 x 14.6 cm) contains the electronics for the video camera and the lightsource, the lightsource itself and connectors for the light guide and videocamera in the specimen stage.

Click picture

Click picture

The specimen stage (27 x 18 x 30.3 cm) provides 4 degrees of freedom for positioning specimens relative to the illumination and the video camera (X,Y,Z-translation and rotation around Z). The design of the stage is such that the rotation is always around the center of the field of view. Additionally the specimen can be rotated independently by rotating the specimenholder.
The stage is designed for quick and reproducible placement of the tissue specimens. A special curtain shields the specimens from ambient light.

The stage comes with specimenholders specially developed to accommodate wide range of tooth-tissue specimens.

S1, the simplest specimenholder provides a flat circular surface to which the tooth specimen can be fixed with putty. Depending on the thickness of the specimen and the amount of putty used to fix the specimen, this specimenholder requires that for each measurement the horizontal and vertical position of the camera must be checked.
To minimize the need for vertical adjustment, S2 was developed. S2 provides a large circular opening that can be filled with putty in which specimens of varying size can be fixed with their surface flush with the top of the specimenholder.

S1 **S2** **S3** **S4**

S3 was made to accommodate relatively large circular enamel slabs (generally bovine) of a fixed size and height, that are routinely used in invitro experiments.
S4 was designed for specimens mounted in perspex (plastic) cylinders. With S3 and S4 type specimenholders, adjustment time of the stage is limited to rotational alignment of successive measurements, which is automatically done by the QLF-InVitro software. The S3 and S4 specimenholders are fitted with a mechanical pin to assist the removal of the specimens after measurement.

It is also possible to request customized specimenholders from Inspektor or to create your own based on one of the available types.

QLF-InVitro software

The PC is fitted with an interface card (frame-grabber) and QLF-InVitro software. Through the interface card, the software displays and captures live video images from the specimen on the stage. When the specimen is correctly positioned and identified, the measurement cycle is started. While gently

The Inspektor crew in front of our Amsterdam location. From left to right, back row: Petra Holland (Industrial design), Esmee Waller (software engineer), Udo Brom (software engineer); middle row: Bart van den Dries (trainee), Elbert Waller (CEO), Monique van der Veen (Senior science officer); front row: Edvins Aritis (software engineer), Anneke Hartmans (Office manager), Elbert de Josselin de Jong (Director R&D). Missing: Moos Dijk (Office assistant)

The Inspektor team (here shown in front of Inspektor's Amsterdam location) is proud to present this attempt to communicate the results of our work to the dental community.

With this newsletter we aim to inform the dental field about our ongoing activities to improve the research, diagnosis and treatment of caries.

Because of our origins in dental research, this first newsletter concentrates mainly on new developments in **research tools.**

Of more general interest may be our report from the NIH **Consensus Conference on Caries Management Throughout Life** that was held in March, 26-28 in Bethesda, Maryland, USA. On this conference, important issues were raised concerning the clinical relevance of caries research.

To brighten up the serious nature of the newsletter, we will also try to report regularly about the glamorous world of dental research in which Inspektor plays its small part.

The newsletter will be available through our website and can also be downloaded for off-line viewing.
The off-line version will also be automatically sent to all our relations whenever it becomes available.
Anybody interested in receiving the newsletter can put his name on the **mailing list** (or remove it) through the same website.

rotating the specimenholder, Inspektor's patented repositioning software automatically selects the image that has the best match with the baseline image. This process typically takes a few seconds and can be repeated if necessary. The resulting image is stored in an experiment database, ordered by specimen-identification and date/time. The specimen can then be replaced in its testing environment.
The analysis software allows the computation of ΔQ values with respect to the baseline image.

Click picture

QLF-InVitro hard- and software requirements
QLF-InVitro will run on any state-of-the-art personal computer that can accommodate Integral FlashPoint framegrabber as its primary display adapter (contact your PC retailer or Integral for more information). Any windows operating system is supported, but QLF-InVitro has been tested extensively with Windows 98 and Windows 2000.
Large amounts of system memory (>128Mb) and disk storage (>40Gb) are recommended. Access to a flexible permanent storage device such as an MO-drive is also advisable.

QLF-InVitro prices
QLF-InVitro is priced at EUR 82.000 (approx. $80.000 USD). This includes all equipment (stage, systembox, PC-interface card), 4 S1-type specimenholders, QLF-InVitro software and 1 day installation, calibration and training. Support by e-mail is provided for 1 year following delivery.

QLF-InVitro availability
QLF-InVitro is now available. Delivery time is 3-6 months. Subject to demand. Contact Inspektor for more information.

TMR for windows NT/2000

Transversal MicroRadiography (TMR) was the first Inspektor product for fundamental caries research. Launched in 1988, under MS-Dos, TMR has evolved steadily into the comprehensive Windows version of today. As the only commercially available, calibrated TMR system, Inspektor's MicroRadiography (IMR) has been adopted by all leading caries research institutes worldwide.
New developments aside, TMR continues to gain popularity in the scientific community. For Inspektor, TMR provides the fundamental basis for all our new quantitative measurement systems.

TMR-2000
TMR is widely used as one of the de facto gold standards for the quantification of mineral loss in dental tissue. Since the launch of the first commercially available TMR system in 1988, Inspektor has continually improved and enhanced its Inspektor MicroRadiography (IMR) line of products. TMR, the most successful product of the IMR line, is now installed in over 10 leading caries-research institutes worldwide, providing reliable and reproducible measurements with a very high comparability between different installations.

To meet the demands of increasing PC performance and evolving operating system development, Inspektor has developed TMR-2000 for windows NT and windows 2000.

TMR-2000 advantages
TMR has been redesigned to comply with the new 32-bit operating system technology and the corresponding hardware. It will now run on the same

The next newsletter will focus on **clinical applications of QLF**. We will try to summarize the current status of the ways QLF can be used in clinical practice. To this end, we have asked pioneers who have applied QLF in clinical settings to review their experiences for us. As an **appetizer**, we have included in the Consensus Conference report a few results from **clinical research** performed by the Medical University of Erfurt, Germany.

Also, we will report about the **IADR** conference in **Tokyo**, Japan and the **ORCA** conference in Graz, Austria, and hope to bring you some visual impressions from this events.

Any **questions** or **remarks** (however scalding) concerning the newsletters, our products or caries research in general are more than welcome. They can be mailed or transmitted by telephone (+31 20 676 4988) or fax (+31 20 679 3183).

With these newsletters we try to transmit Inspektor's commitment towards the improvement of caries detection and treatment. We believe that important new developments are due in the near future, that will seriously affect the ways that caries is diagnosed and treated.

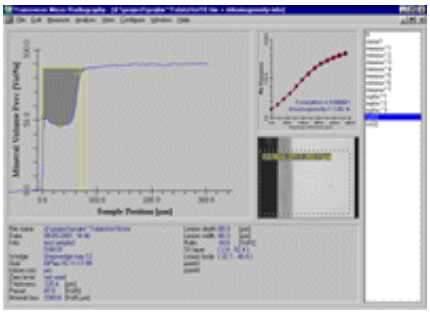
We hope that this newsletter will contribute to the dissemination of information about these developments and that its contents will be informative to the dental community.
We are looking forward to your reactions.

NIH pictures

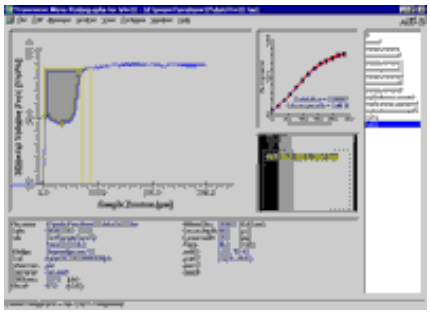
hardware used by QLF, reducing the need to maintain different hardware configurations for Inspektor's product line for fundamental caries research. This redesign has also been used to increase the reliability of the program and to revamp the user-interface while retaining the familiar look and feel of the 16-bit version of TMR.

TMR-2000 compatibility

TMR-2000 is fully compatible with earlier versions. A typical comparison is shown below, where the same microradiogram was analyzed using both the 16-bit version of TMR and TMR-2000.



TMR 16 bit



TMR-2000

These results demonstrate the very high correspondence of the two versions. This is especially impressive because these measurements were made with completely different hardware and include manual positioning of the start of the enamel and the level of sound enamel. (The critical reader will also observe that the TMR-2000 graph contains significantly more noise than the graph of TMR-16. This was due to the use of a rather old video camera for the TMR-2000 measurement.)
Also, measurements done with the 16-bit version are 'upwards compatible' with TMR-2000. This means that your existing TMR measurement database can blend in seamlessly with TMR-2000 measurements.

TMR-2000 hard- and software requirements

TMR-2000 will run on any state-of-the-art personal computer running any of the 32-bit compatible windows operating systems (W98, ME, WANT, W2000) that can accommodate the Integral FlashPoint framegrabber as its primary display adapter (contact your PC retailer or Integral for more information).

TMR-2000 availability and pricing

TMR-2000 is now available. Due to the specialized nature of each TMR system, no general pricing information is available. For a personalized quote, please contact Elbert de Josselin de Jong or Anneke Hartmans at Inspektor.

NIH Consensus Conference

On March 26-28, 2001, the NIH Consensus Conference on Diagnosis and Management of Caries Throughout Life was held at the NIH Natcher Conference Center in Bethesda, Maryland, USA. The aim of the conference was to evaluate past dental research and identify new and promising technologies focused on caries prevention and diagnosis. Inspektor, as a leading manufacturer of caries detection methods, was represented by its presidents, Elbert de Josselin de Jong and Elbert Waller, and by its senior scientific officer, Monique van der Veen.

OHRI's George Stookey and Aine Lennon discussing caries and hot whiskey.

Inspektor's Elbert de Josselin de Jong trying to spot a customer outside Natcher Conference Center.

OHRI's Aine Lennon and Inspektor's Monique van der Veen and Elbert de Josselin de Jong pondering the impact of NIH parking instructions on the spread of infectious diseases.

NIH: Conference report

This article will focus on some of the highlights of the conference. For a full report, including the final consensus paper, see the NIH consensus site.

The conference took one and a half day and was very well attended despite the cold, but very fair weather. The program was extensive resulting in fast speakers and a weary audience. Many subjects were brought forward at breakneck speed, examined quickly and relentlessly only to be replaced by the next speaker for the full duration of the conference.

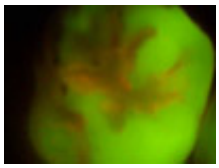


Fig 1. QLF image of fissure covered with a thick layer of plaque.

Gloom sometimes threatened the congregation as one speaker after the other declared yet another realm of caries research to be unable to stand up to the rigorous demands of systematic review, as defended by its chief-inquisitor **James Bader**.

Relief was brought by **Nigel Pitts**, who harassed his hosts with the European aversion to tactile examination (**examiner bashing**) and was happily provided with some heated response.

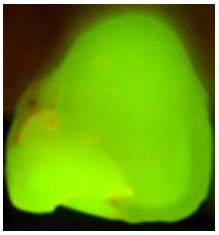


Fig 2. QLF image of failure of composite restoration.

As it turned out, many of the seemingly bleak results brought forward by the systematic review could be partly explained by the in- and exclusion criteria wielded by the executioners which did not match the general study paradigm of the period considered.
However, it was clear that the subjective nature of visual inspection and the insensitivity of visual examination when applied to early caries lesions was one of the most damaging factors for the analysis power of many studies.

To Inspektor, the first half of the conference concerning caries diagnosis and risk assessment was probably the most interesting. Not unexpectedly, considering caries diagnosis is primarily done using visual examination that can only detect caries in its final stages, **past caries experience** proved to be the best predictor for **caries risk**.
The most important **conclusion** of the conference was that, because caries is an infectious disease, there is a need to identify the **infection** rather than the symptoms (lesions) as early as possible.

NIH: Inspektor views

For Inspektor, one of the most interesting issues was the vision of the conference towards caries detection and especially on the relation that is perceived between frank lesions and the early caries process and the detection of **active infections**.

Early caries lesions: are they relevant?

Many people, dentists and dental manufacturers among them, have strong doubts about the clinical relevance of early caries lesions. They base their doubt on the observation that **only about 10%** of early caries lesions ever develop into frank lesions.
In their reasoning, looking at very early caries lesions will just confuse matters when looking at clinical effects of treatments or dental products. They believe that many of these early lesions will never develop to frank lesions anyway, whether they are influenced by a treatment or not. Therefore, their position is that any change of an early lesion might prove to be insignificant in the long term. In which case the proven visual inspection might as well be

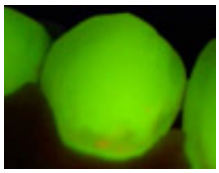


Fig 3. QLF image of an active early lesion along the gingiva after orthodontic treatment

Monique van der Veen and Elbert de Josselin de Jong ruminating about new QLF strategies.

Elbert de Josselin de Jong explaining his position in the intercontinental examiner debate.

used.

We think they are relevant ...

Although we do not think that measuring early caries lesions can instantly replace the old and proven ways, the fact remains, that any **frank caries** lesion **starts off** as an early lesion that can be **arrested**. For the first time in the history of dentistry, it is now possible to **follow** the caries process from its **very beginning**, in the mouth, using Quantitative Light-induced Fluorescence (QLF).

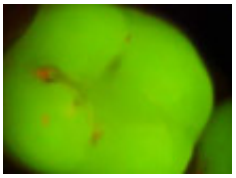


Fig 4. QLF image showing small active lesions in the region of the occlusal surface with partial loss of fissure sealant.

Ongoing and future research will focus on **monitoring** early caries lesions, identifying active lesions, studying the effects of treatments and products on these lesions and deepening our understanding of the development of the caries process in vivo.

We believe that anyone who is seriously interested in the **treatment** and **prevention** of caries can not ignore this opportunity and the new insights it will bring. From the enhanced understanding of the early caries process and its relation to the development or prevention of frank lesions, new approaches will arise to measure and evaluate efficacy of treatments and products.

NIH: $6 M support for QLF-validation

One of the conclusions of the Consensus Conference was that there is a need for better objective diagnostic methods that will improve inter-examiner consistency.

Of the currently available technologies, we believe only QLF is ready to be introduced into clinical practice and able to meet these needs.

Happily, we are not alone in this. The **NIH/NIDCR** has awarded a **$6.000.000 grant** for validation and evaluation studies, recognizing the potential of QLF and other emerging technologies for an impact on preventive dentistry.

Many leading caries researchers share our enthusiasm for **QLF** and are actively researching the validity and the possibilities of the technology.

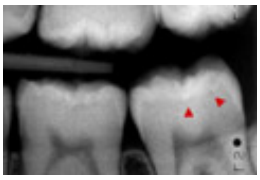


Fig 5a. Bitewing corresponding to the QLF-image on the right. The red arrows indicate a radiolucency in the dentine.

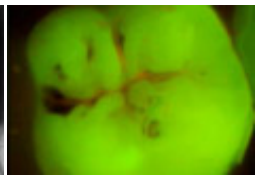


Fig 5b. Demineralized and bacterially infected fissure; the distal fissure displays dentinal caries with a small surface cavity.

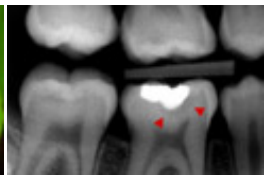


Fig 6a. Bitewing of a amalgam filling with secondary caries that was replaced with a composite filling.

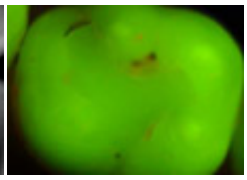


Fig 6b. QLF image of composite filling that replaced the amalgam filling in the bitewing on the right, showing that not all secondary caries was removed.

(All pictures courtesy of the faculty of Preventive Dentistry of the Medical University of Erfurt, Germany. Images 1-4 were captured by Roswitha Heinrich-Weltzien. Images 5ab and 6ab were captured by Jan Kühnish)

Pushing the envelope

We believe that dental caries research is in for a rather spectacular revival.

Inspektor has committed itself to push the exploration of this field. This month saw the launching of the QLF-InVitro system, described elsewhere in this newsletter, to support and facilitate fundamental research. And we keep improving on trusted technology such as TMR to provide QLF with a solid empirical basis.

We are actively working on the introduction of the QLF-InVivo camera to the clinic and to reduce the cost and the effort needed to put it to good clinical use.
New, breakthrough work is being done to distinguish active lesions from inactive ones. This leads to results that we believe will be used to detect and quantify points of infection in the mouth and will be a significant step forward towards early detection and treatment as stipulated by the Consensus Conference.