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Views from World Leaders in Operative Dentistry

Finished the tooth preparation, now what?

Challenges in dental adhesion:
Novel strategies and ongoing research

Cristina Vidal & Ariene Leme-Kraus
June 10, 2022

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Disclosure

We do **NOT** have any conflict of interest with organizations

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Learning objectives

Participants should be able to:

→ Recognize changes within the dentin substrate that can affect the performance of current adhesive materials

→ Explain the contribution of the dentin matrix biomechanics and stability (at macro- and nano-scale) to the failure of the adhesive restorations as well as its degradation mechanisms

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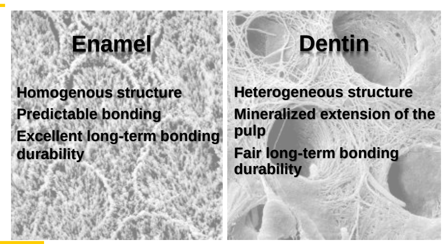
Dental substrates



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1. Understanding sound/healthy dentin and the roles of its different components when stablishing predictable tooth-dental adhesive joints

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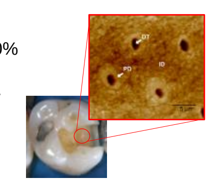
Dentin aspects relevant to adhesion and biomechanics

→ Dentin: Calcified tissue - bulk of the tooth.

→ Composition by vol. 50% mineral phase, 40% organic phase and 10% water.

→ Morphology: Intertubular dentin, peritubular dentin and dentin tubules.

- Increased tubule density closer to the pulp – increased moisture.



Habelitz et al., 2002; Bedran-Russo et al., 2014

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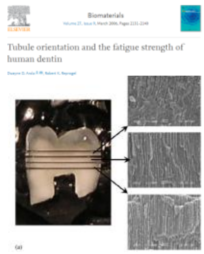
Dentin aspects relevant to adhesion and biomechanics

- Proximity to pulp – More superficial region tubule density **9,400** tubules/mm^2

  Middle region tubule density **37,800** tubules/mm^2

  Cervical (deep) region tubule density **51,400** tubules/mm^2



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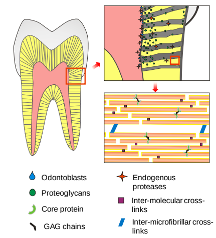
Dentin aspects relevant to adhesion and biomechanics

- Organic phase or dentin extracellular matrix (ECM) – collagen and non-collagenous proteins
  - Type I collagen – (90%wt.) organized hierarchically
    - Collagen molecule (triple helix), microfibrils, fibrils
    - Cross-links stabilize the structure
  - Proteoglycans – 3% vol.
    - Protein core attached to glycosaminoglycan (GAGs)
    - Hydrophilic
    - Sliding between fibrils



Habelitz et al., 2002, Bertassoni 2017, Vidal et al., 2017

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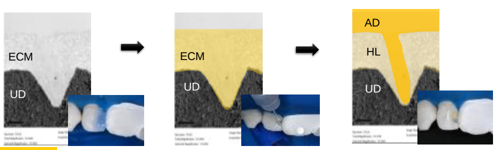
Adhesive strategy – Dentin

- Dentin is a more challenging adhesive substrate.
- Dentin-resin interface – multilayered structure (adhesive, hybrid layer and underlying dentin).
  - Resin monomers infiltrate and fill the spaces formerly occupied by minerals.



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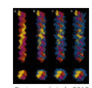
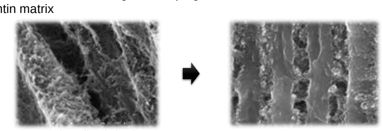
Roles of water in the adhesion to dentin

- Bound and unbound water within collagen
  - Wet bond technique – etch-and-rinse and universal adhesive systems
  - Resin infiltration – wet demineralized dentin
    - Water H-bonds with collagen – keeping the structure of the demineralized dentin matrix



Bertassoni et al., 2012.



Demineralized dentin

Resin-infiltrated dentin

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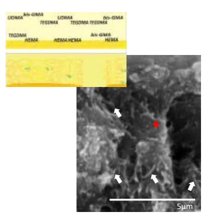
Roles of water in the adhesion to dentin

- Current adhesive systems
  - Organic solvents – acetone, ETOH/H_2O complexes.
  - Hydrophilic monomers – HEMA
    - Susceptible to degradation, diffusion within the dentin matrix.
  - Hydrophobic monomers and photo initiators stay on top.

Abedin et al., 2015



Hybrid layer and resin tag
Areas of unprotected collagen

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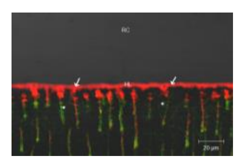
Roles of water in the adhesion to dentin

- Micropermeability of the dentin-resin adhesive interface.
  - Water molecules within the hybrid layer.
- Demineralized and unprotected collagen underneath the hybrid layer.
- Paths for continuous degradation of the dentin-resin interface.



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Dentin permeability and hydraulic conductance

- Ideally:
  - Resin monomers will replace all the unbound water within the dentin matrix and polymerize.
- We should always consider dentin permeability:
  - Caries management.
  - Proximity to pulp:
    - Postoperative sensitivity;
    - Toxicity of adhesive systems.

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Resin-infiltrated dentin and failure mechanisms

- Fracture behavior within the dentin-resin infiltrated dentin-composite zone


A comparison of fatigue crack growth in resin composite, dentin and the interface


Journal of Biomechanics
Potential role of surface wettability on the long-term stability of dentin bonds after surface biomodification

- Dentin-resin adhesive interface is more sensitive to fatigue crack growth than either dentin or resin composite
- Difference in modulus of elasticity (by nanoindentation) of the adhesive, hybrid and underlying dentin layers

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2. Changes in carious and non-carious dentin relevant to adhesion

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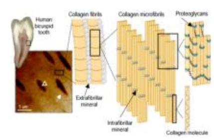
Physiological dentin aging


Acta Biomaterialia

- Aging within the coronal dentin:
  - Decreased damping capacity of the coronal dentin.
    - Negatively affecting strength, toughness and fatigue resistance.
- What causes the dentin to age?
  - Physiological aging
    - Continuous mineral deposition
    - Aging of the dentin extracellular matrix
  - Stress induced aging
    - Repeated excessive/eccentric loading - NCCLs
    - Caries



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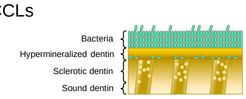
Sclerotic dentin in NCCLs

- Non-carious cervical lesions - NCCLs
  - Abfraction lesions
  - Hypermineralized dentin layer
  - Mineral-dense sclerotic casts



- Selective etching when using universal adhesive systems
- Extension of the gingival recession towards the root apex may influence the lifespan of the restoration

Tay FR, Pashley DH, 2004.
Perdigão J. 2010.

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Bonding to Sclerotic Dentin


Meta-Analysis of the Influence of Bonding Parameters on the Clinical Outcome of Tooth-colored Cervical Restorations
Eduardo Mahn / Valentin Rousson / Siegward Heintze

- Class V restorations (NCCLs)
- After 8 years:
  - Retention rate: 76.2%
  - Without marginal discoloration/detectable margins: 67.7%
- Roughening of the surface and rubber dam resulted in better retention
- Bevel on enamel did not affect retention rates of resin composite restorations but worsened the performance of glass ionomer restorations

Mahn et al., 2015, Journal of Adhesive Dentistry

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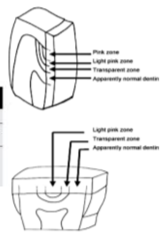
Bonding to Intact vs. Carious Dentin

- Carious dentin is the most common bonding substrate
- Adhesion to carious dentin results in THICK hybrid layers and low bond strength

Table 1 – Comparison of the thickness of the hybrid layer: mean ± S.D. (μm) of each group, by adhesive, orientation of dentin tubules and zone of carious dentin

Zone of caries dentin	Parallel group (n=5)		Perpendicular group (n=5)	
	SE Bond adhesive	3M Single Bond Plus adhesive	SE Bond adhesive	3M Single Bond Plus adhesive
Pink zone	8.5 ± 7.5	7.9 ± 3.6 ^{a}	22.4 ± 12.8 ^{c}	20.8 ± 6.3 ^{a,c}
Light pink zone	3.5 ± 1.8	7.2 ± 3.5	3.7 ± 1.8 ^{b}	8.6 ± 2.5 ^{c}
Transparent zone	1.6 ± 0.5 ^{b}	4.1 ± 0.7 ^{b}	1.5 ± 0.8 ^{b}	5.1 ± 0.9 ^{b}
Apparent normal dentin zone	1.0 ± 0.4 ^{b}	3.5 ± 0.6 ^{b}	0.8 ± 0.3 ^{b}	3.7 ± 0.7 ^{b}

Hsu et al. Dental Materials 2008



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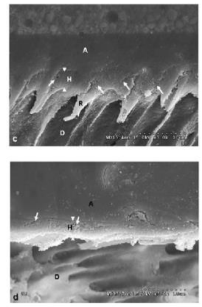
Bonding to Intact vs Carious Dentin

- Bond strength is inversely proportional to the degree of caries progression
- Adhesives infiltrate carious dentin more fully (increased permeability)
- There is no correlation between HL thickness and bond strength in sound teeth – in carious is about the QUALITY of the HL

Carious dentin: increased water content, porosity, and permeability

HL presents cracks and pores (arrows SEM images)

Hsu et al. Dental Materials 2008



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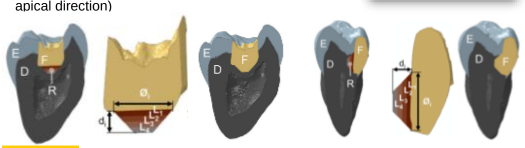
Besides the HL…changes in biomechanics

- 3D-FE class I and II with variable sizes with full or selective caries removal on occlusal and proximal surfaces
- Vertical force (100N) applied to the occlusal (occluso-apical direction)



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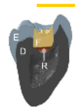
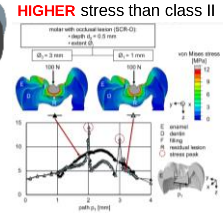
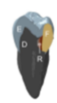
Besides the HL…changes in biomechanics



HIGHER stress than class II





LOWER stress than class I
Extensive lesions -> higher stress in proximity to the occlusal surface

Lesion depth **does not** influence stress around restoration-dentin interface
Anatomical site and extent of the lesion are the decisive factors that should be considered

Weimann et al., 2021

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3. Longevity of adhesive restorations

Hybrid layer degradation mechanisms
How to improve bond durability

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Problems of contemporary adhesive systems

- Performance is material-dependent
- Do not present the same potential to bond to enamel AND dentin AND other substrates
- Sensitive to hydrolytic degradation (mainly functional monomers and systems with high water content)

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Failure of Adhesive Restorations

Factors that compromise the durability of resin-dentin bonds:

1. Water sorption with hydrolytic degradation of the adhesive and resin
2. Enzymatic biodegradation of the dentin by endogenous and exogenous enzymes

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Role of water on the aging of dentin-resin interfaces

→ Degradation of the hybrid layer and underlying dentin after 30 months
- Top of the adhesive interface remained stable
- Nanomechanics of the interface – site-specific properties

→ Hydrophilicity of the demineralized dentin was reduced following biomodification (Glutaraldehyde, EDC/NHS and Grape seed extract)

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Table 1
Summary of the contributors and the mechanism of the degradation of adhesive interfaces

Structure/Material		Characteristic/ Mechanism	Result	Contribution to Failure
Dental resins	Resin composite	Rough surface Leached/ unreacted resins	Favors biofilm formation and growth Favors acidogenic biofilm	Resin degradation by esterases Secondary caries Increases interfacial porosity
	Adhesive system	Unreacted/ leached resins	Increase water/ saliva sorption Hydrolysis of resin Reach pulp tissue	Pulp response Susceptibility to degradation
		Incomplete monomer infiltration	Exposed dentin organic matrix	Enzymes degrade anchoring collagen
		Etching technique/pH	Activation of endogenous proteases[a]	Loss of interfacial bonding/seal
Dental tissues	Latent endogenous proteases[a]	Latent enzymes activate at low pH	Degradation of dentin matrix	Increases interfacial porosities
	Inherent moisture	Water trapped at the adhesive interface	Hydrolysis of resin	Loss of interfacial bonding or seal
Oral environment	Bacterial esterases Salivary esterases	Enzymatic activity Enzymatic activity	Resin polymer degradation and release of monomers and byproducts	Enzymes degrade anchoring collagen Increases interfacial porosities
	Biofilm	Leached or unreacted resins	Favors biofilm formation and growth Favors acidogenic biofilm	Loss of interfacial bonding/seal Secondary caries

An Overview of Dental Adhesive Systems and the Dynamic Tooth–Adhesive Interface

Ana Bedran-Russo, DDS, MS, PhD[a,*], Ariene A. Leme-Kraus, DDS, MS, PhD[b], Cristina M.P. Vidal, DDS, MS, PhD[c], Erica C. Teixeira, DDS, MS, PhD[c]

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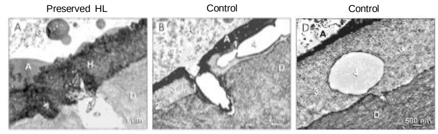
Degradation of hybrid layer by endogenous/exogenous enzymes

Preserved HL — Control — Control



MMPs and cathepsins are **acid-activated and degrade exposed collagen**
Once collagen is disorganized/partially degraded, its complete degradation would be mediated by endogenous and exogenous enzymes

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Dentin degradation: Intact vs. Carious

→ Most *in vitro* studies use intact dentin (or NCCLs *in vivo*)

→ Studies suggest more intense degradation of carious dentin HL: altered collagen, increased water content, water sorption and permeability, low degree of resin monomer conversion

→ Bonding to caries affected dentin needs to be further understood

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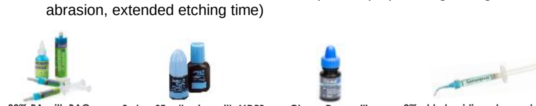
How to improve bond durability

→ Proper selective removal of caries
→ Field isolation
→ Surface treatment? (glutaraldehyde, proteolytic inhibitors (chlorhexidine), antibacterial adhesive systems, collagen cross-linkers/dentin biomodification)
→ Surface treatment for altered substrates (NCCLs)? (bur roughening, air abrasion, extended etching time)



32% PA with BAC Uni-etch (Bisco) — 2-step SE adhesive with MDPB Clearfil Protect Bond (Kuraray) — Gluma Desensitizer (Kulzer) — 2% chlorhexidine gluconate solution Consepsis (Ultradent)

Images from manufacturer website

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Selective removal of caries

- Concept of adequate peripheral seal for caries management
- Adequate marginal sealing while being less invasive
- Enamel margins and hard dentin at the periphery with a clean DEJ
- Selective caries removal centrally to firm/leathery dentin

de Almeida Neves A et al., J Adhes Dent. 2011

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Rubber dam isolation

- 4 studies that analyzed 1270 participants
- Even thought included studies were at high risk of bias, use of rubber dam isolation resulted in higher survival rate than cotton roll isolation at 6-months (NCCLs)


Cochrane Library
[Intervention Review]
Rubber dam isolation for restorative treatment in dental patients

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Rubber dam isolation and contamination

Contamination during bonding procedure

Contamination with saliva and/or other fluids (blood) results in reduced bond strength of composite to tooth structure, especially if occurs during primer application or before LC

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Rubber dam isolation and contamination

- Decontamination: repeat bonding procedure?
- Wash, dry, repeat adhesive application

(Pappa et al. Gen Dent. 2022; 70(3):22-26)

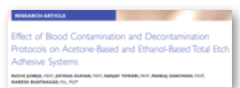
RESEARCH ARTICLE
Effect of Blood Contamination and Decontamination Protocols on Acetone-Based and Ethanol-Based Total Etch Adhesive Systems

TABLE 2. Microtensile bond strengths for Prime & Bond NT and Single Bond with different decontamination protocols tested (mean ± standard deviation, MPa)

Group	Prime and Bond NT	Single Bond
Group 1: Control	24.4 (2.8)	24.7 (3.2)
Group 2: No rinsing	12.1 (6.9)	15.1 (3.5)
Group 3: Water rinsing	18.0 (2.7)	18.2 (3.2)
Group 4: Re-etching	19.6 (4.2)	23.3 (2.5)
Group 5: Sodium hypochlorite	21.1 (5.7)	18.5 (8.0)
Group 6: NaOCl + Ascorbate	24.3 (3.9)	20.2 (8.6)
Group 7: Hydrogen peroxide	15.1 (8.0)	17.8 (7.3)
Group 8: Ethanol	13.5 (7.5)	15.2 (5.3)

Mean values ± standard deviation followed by different superscript in the column differ statistically among themselves for the Tukey test at the level of 5%.

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Substrate contamination

- Contamination by hemostatic agents affects bonding
- Bond strength of self-etching adhesive systems is affected more negatively than is that of etch-and-rinse systems


The influence of hemostatic agents on dentin and enamel surfaces and dental bonding
A systematic review

Image: Ultradent website

Why? Coagulation of plasma proteins in the dentinal fluid, contaminants present in the gels/solutions

Etching using phosphoric acid for 15 s followed by a water spray was an effective cleaning method

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Surface Treatment


Journal of Dentistry

- Glutaraldehyde
  - Biological tissue fixative
  - Promotes collagen cross-linking in dentin
  - May block tubular flow *in vitro* – protein precipitation in the tubules
  - Conflicting results on its efficacy in reducing post-op sensitivity

No reduction in spontaneous or stimulated post-op sensitivity of posterior resin restorations (universal adhesive using SE and E&R)

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Antibacterial adhesives

- Important to consider short-term and long-term effects
- Incorporation of quaternary ammonium methacrylate MDPB, glutaraldehyde, benzalkonium chloride (BAC), CHX, silver nanoparticles, dentin biomodifiers (EGCG), DMSO

Universal adhesives: Higher bond strength of UAs modified with antibacterial materials
(high heterogeneity 92%)
No effect on inhibition of *S. mutans*
Non-modified UAs also promote bacteria inhibition due to low pH


microorganisms
Review
The Bond Strength and Antibacterial Activity of the Universal Dentin Bonding System: A Systematic Review and Meta-Analysis

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Cavity disinfection

- Commonly used: CHX and NaOCl (Gluma and BAC also included)
- CHX: maintained or increased bond strength in most of the *in vitro* studies
- Possible negative effects when combined with self-etching system
- Use of NaOCl is not supported
- CHX is a safe option, positive results in several *in vitro* and *in situ* studies

Evidence to support its clinical use?


International Journal of Molecular Sciences
Review
Effect of Cavity Disinfectants on Dentin Bond Strength and Clinical Success of Composite Restorations—A Systematic Review of In Vitro, In Situ and Clinical Studies

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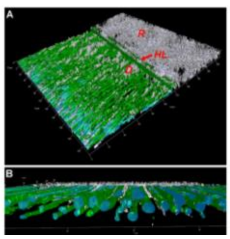
Proteolytic inhibitors

- Activity of MMPs is dependent on metal ions
- Inhibitors that act by a chelating mechanism: CHX, EDTA, quaternary ammonium compounds (BAC and MDPB)
- Specific inhibitors of MMPs and cathepsins (Galardin, E-64, *in vitro* studies only)


32% PA with BAC Uni-etch (Bisco)
Clearfil Protect Bond (Kuraray)
2% CHX gluconate Consepsis (Ultradent)



Breschi et al. Dental Materials, 2018

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Effectiveness of CHX pre-treatment: *in vitro* studies

- Meta-analysis included 21 studies using 0.2 – 2% CHX in the bonding procedure
- *In vitro* studies evaluating immediate and long-term bond strength
- Significantly higher bond strength after 6, 12, and 24 months of aging when CHX was used


Review Article
MMP Inhibitors and Dentin Bonding: Systematic Review and Meta-Analysis
O. Kiuru, J. Sinervo, H. Vähänikkilä, V. Anttonen, and L. Tjäderhane

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Effectiveness of CHX pre-treatment: *in vitro* studies

- Proteolytic inhibitors applied on caries affected dentin did not improve bond strength when associated to a universal bonding system after 18 months
- Carious substrate was the worst substrate to bond
- CHX associated with 10-MDP based system notably compromised bonding durability


Journal of the Mechanical Behavior of Biomedical Materials
Performance of MDP-based system in eroded and carious dentin associated with proteolytic inhibitors: 18-Month exploratory study

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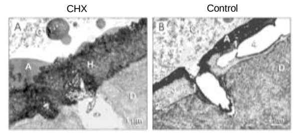
Effectiveness of CHX pre-treatment: *in vivo* studies

CHX Control



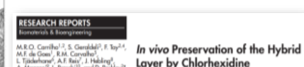

RESEARCH REPORTS
Biomaterials & Bioengineering
M.R.O. Carrilho[1,2], S. Geraldeli[3], F. Tay[2,4], M.F. de Goes[1], R.M. Carvalho[5], L. Tjäderhane[6], A.F. Reis[7], J. Hebling[8], A. Mazzoni[9], L. Breschi[10], and D. Pashley[2]*
***In vivo* Preservation of the Hybrid Layer by Chlorhexidine**

Table. Bond Strength and Distribution of Failure Modes of *in vivo* Resin-Dentin Bonds

	Bond Strength (MPa)*		Failure Modes (%)**	
	Immediate	14 mos	Immediate	14 mos
Control	29.3 ± 9.2 (14)[A]	19.0 ± 5.2 (34)[B]	20% CRB; 15% CHL, 65% M	5% CBR; 30% CHL, 10% CD; 55% M
CHX	32.7 ± 7.6 (17)[A]	32.2 ± 7.2 (32)[A]	15% CBR; 30% CHL, 55% M	10% CRB; 30% CRC; 20% CHL, 40% M

* Bond strength values are means ± standard deviations (n = beams/group). Different superscripts indicate statistically significant differences ($p < 0.05$).
** Failure mode abbreviations: CRB, cohesive failure in bonding resin; CHL, cohesive failure in the hybrid layer; CD, cohesive failure in dentin; CRC, cohesive failure in resin composite; M, mixed failure. There were no premature failures of specimens during testing.

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Effectiveness of CHX and other inhibitors of HL degradation: *in vivo* studies

Clinical significance: Current scientific evidence cannot neither strongly recommend nor discourage the application of CHX as therapeutic primer in composite restorations. Studies with longer follow-up periods with adhesive restorations placed on dentin after caries removal, rather than only on NCCL, are desirable to further investigate the therapeutic effect of CHX during bonding procedures.

In conclusion, there is insufficient evidence to recommend or refute hybrid layer degradation inhibitory cavity pretreatment prior adhesively placing resin-based restorations. Based on this review and the included studies, dentists could pretreat cavities prior adhesively placing restorations (for example as part of re-wetting the cavity, or introduced to an adhesive), while evidence supporting this strategy is lacking. The impact of further effects (e.g. disinfection, pulp-irritation) of pretreatment remains unclear.

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Dentin Biomodification

Biomimetic approach mediated by bioactive agents to enhance and reinforce the dentin by locally changing **the biochemistry and biomechanical properties**.

Interaction of bioactive agents with **different components** of the ECM

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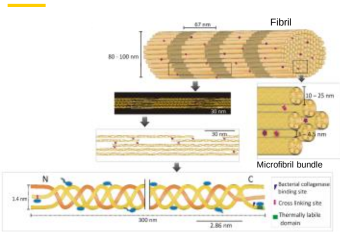
Dentin Biomodification



Collagen cross-links
Inter-microfibrillar
Inter-molecular
Intra-molecular

Inhibition of proteolytic enzymes

Interaction with other components of the ECM

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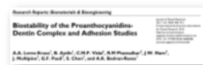
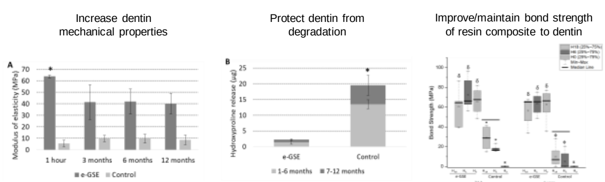
Dentin Biomodification



→Bioactive compounds (proanthocyanidins, GSE):



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Even more important in adhesion to carious dentin?

Table 1: *Secondary Caries Lesions Depth and Total Fluorescence Calculated by Area and Distances From the Dentin and Enamel Margins*[a]

Cavity primers	Margins in dentin: Lesion depth (µm)	Margins in dentin: Total fluorescence (×10⁵), mean (SD) 250 µm	100 µm	50 µm	25 µm	Margins in enamel: Lesion depth (µm)	Margins in enamel: Total fluorescence (×10⁵), mean (SD) 250 µm	25 µm
Control	72.5 (9.8)	8.06 a (5.51)	3.37 ab (1.98)	1.82 ab (1.04)	1.04 b (0.57)	80.5 (29.7)	6.20 (6.93)	4.16 (3.71)
e-GSE	74.8 (15.0)	8.23 a (5.57)	2.29 a (1.63)	0.79 a (0.70)	0.27 a (0.30)	67.8 (18.7)	4.06 (3.50)	2.20 (1.37)
EDC/NHS	71.2 (16.4)	10.75 a (6.78)	4.45 ab (3.14)	2.29 ab (2.05)	1.24 b (1.14)	71.7 (22.6)	2.42 (3.90)	2.40 (2.79)
CHX	74.4 (13.1)	12.29 a (6.27)	4.86 b (2.85)	2.69 b (1.81)	1.37 b (0.83)	83.4 (49.3)	5.55 (6.43)	3.21 (3.12)

[a] *Different letters indicate statistically significant differences in each column ($p<0.05$).*

Compared PACs (e-GSE) with EDC/NHS (collagen cross-linker) and CHX

Secondary caries development at the margin was inhibited by e-GSE ONLY

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What does the future hold for dental adhesives?

- Continue to improve formulations to allow less steps and easy application (less technique sensitive)
- Sophisticated mixtures to promote bonding to all substrates and facilitate repairs
- Bioactive/therapeutic adhesives (antimicrobial, anti-enzymatic, remineralization, nanotubes, nanoparticles, novel monomers)
- Self-adhering restorative materials

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THANK YOU!

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