Table S1. Materials and devices used within the study.

Material	Manufacturer	Composition	Preparation/Application Procedure
Biodentine™	Saint-Maur-des-Fossés Cedex, France	***Powder:*** Tricalcium silicate, zirconium oxide, calcium oxide, calcium carbonate, and colourings. ***Aqueous solution:*** Calcium chloride and polycarboxylate.	1) Gently tapping the capsule on a hard surface 2) Pouring of 5 drops from single-dose container into the capsule 3) Closing of capsule, placing capsule into mixing device (CapMix) for 30 seconds
SDR™	Dentsply DeTrey, Konstanz, Germany	Barium-alumino-fluoroborosilicate glass, strontiumalumino-fluoro-silicate glass, modified urethane, dimethacrylate resin, EBPADMA, TEGDMA, CQ, photoaccelerator, BHT, UV stabilizer, titanium dioxide, iron oxide pigments, fluorescing agent	1) Dispense SDR™ in layers of maximum 4 mm 2) Light-curing for at least 20 seconds per layer
CeramX™	Dentsply DeTrey, Konstanz, Germany	Ethoxylated Bisphenol A Dimethacrylate, Urethane modified Bis-GMA dimethacrylate resin, 2,2´-ethylenedioxydiethyl dimetharcylate, ytterbium trifluoride, 2,6-di-tert-butyl-p-cresol	1) Application of material in increments up to a thickness of 2 mm 2) Light-curing of each increment for at least 20 seconds 3) Finishing and polishing
Guttapercha Beefill Cartridge	VDW Dental, Munich, Germany	Zinc oxide, guttapercha, barium, sulfate, wax, composites, colourings	1) Application of thermo-plasticized guttapercha on a spatula 2) Rapid adaption on the residual carious dentin nearby the pulp
Optibond™ FL	Kerr GmbH, Biberach, Germany	***Primer:*** Ethanol, ethylethanol, 2-Hydroxyethylmethacrylate, GPDM, PAMA, water, Camphorquinone ***Bond:*** Bisphenol-A-dimethacrylate, 2-Hydroxyethylmethacrylate (HEMA), Triethylenglycoldimethacrylate, 3-Methacrylolyl-oxypropyltrimethoxy-silane, Ba-Al silica glass, Camphorquinone, Na_2SiF_6	1) Etching with phosphoric acid (37%) for 20 seconds 2) Rinsing with water for 15 seconds 3) mild air flow for drying for 5 seconds 4) Gently application of primer for 15seconds 5) mild air flow for 5 seconds 6) Application of bond 7) Light curing for 30 seconds
Clearfil™ SE Bond 2	Kuraray Noritake Dental Corporation, Okayama, Japan	***Primer:*** MDP, HEMA, Hydrophobic dimethacrylate. N-Diethanol-p-toluidine, amphorquinone, water ***Bond:*** MDP, Bis-GMA, HEMA, silanated colloidal silica, hydrophobic dimethacrylate, Camphorquinone, water, N-Diethanol-p-toluidine	1) Gently application of primer for 20 seconds 2) Mild air flow for drying for 10 seconds 3) Application of bond 4) Gently air flow 5) Light curing for 10 seconds
Clearfil™ Protect Bond	Kuraray Noritake Dental Corporation, Okayama, Japan	***Primer:*** water, MDP, MDPB, HEMA, hydrophobic methacrylate ***Bond:*** MDP, DEMA, Bis-GMA, hydrophobic dimethacrylate, di-Camphorquinone, N-Diethanol-p-toluidine, silanated colloidal silica	1) Gently application of primer for 20 seconds 2) Mild air flow for drying for 10 seconds 3) Application of bond 4) Gently air flow 5) Light curing for 10 seconds
Opaldam	Ultradent Products, South Jordan, USA	Cetylalkohol, Diurethan-dimethacrylate	1) Application of the material in case of problems to seals the cavity with the matrix properly 2) Light-curing for at least 20 seconds
PBST (10X)	G-Biosciences GmbH, St. Louis, USA	80mM Na 2 HPO 4, 1.5M NaCl, 20mM KH 2 PO 4, 30mM KCl, 0.5% Tween® 20, pH 7.4.	1) Filling the prepared cavity with PBST 2) Incubating for 5 minutes

	3) Regaining of fluid with a 200 µl microtiter pipette

Table S2. Quantitative evaluation of pro-inflammatory cytokines when all groups were pooled and differentiated for the single interventional groups: guttapercha (GP), Biodentine (BD), Clearfil Protect Bond (PB), Clearfil SE Bond 2 (SE) (median, maximum, minimum; concentration, pg/mL).

LegendPlex Panel (BioLegend GmbH, Koblenz, Germany)	Analysis of IL-1β, IL-6, IL-10, CRP, TNF-α, IFN-γ, TIMP-1, TIMP-2

- preparation of the masterplate (96 well plate), dilutions were performed on second 96 well plate (1:1 dilution, sample volume 30µl + assay buffer 30µl)
- preparation of wash buffer: 47.5 mL deionized water + 2.5 mL wash buffer 20X
- preparation of matrix: lyophilized matrix + 5 mL assay buffer (vortex!)
- preparation of standard: lyophilized standard cocktail + 250 µL assay buffer
  - standard = C7, labelling of tubes C7- C0
  - addition of 75 µL of assay buffer to C6-C1, preparation of 1:4 dilution transferring 25µl of the standard

The entire assay was performed on a filter-well plate.

- addition of 100 µL wash buffer to filter plate, let sit for 1 min at room temperature
- centrifugation for 30 seconds at 300 rpm, flow through discarded
- addition of 25 µL of assay buffer to the sample wells
- addition of 25 µL of matrix to the standard wells
- addition of 25 µL of each standard to the standard wells
- addition of 25 µL of each diluted sample to the sample wells and vortex
- addition of 25 µL beads to each well (volume should be 75 µL in each well)
- overnight on a plate shaker (500 rpm 4 °C), sealing the plate with aluminium foil
- next day: centrifugation 30 seconds, 300 rpm, flow through discarded
- addition of 200 µL wash buffer to each well and centrifugation 30 seconds, 300 rpm to remove wash buffer, repetition
- addition of 25 µL detection antibodies (biotinylated) to each well, sealing the plate with aluminum foil
- shaking for 30 min 500 rpm at room temperature
- addition of 25 µL of SA-PE to each well and sealing the plate with aluminium foil
- shaking for 30 min 500 rpm at room temperature on a plate shaker, centrifugation 30 seconds at 300 rpm, flow through discarded
- addition of 200 µL wash buffer to each well, centrifugation 30 seconds at 300 rpm to remove wash buffer, repetition
- addition of 150 µL wash buffer to each wellse
- reading samples on flow cytometer with 300 events per cytokine, thus 1500 events

Human Custom 3-Plex assay (Aimplex Biosciences, Inc., Pomona, USA)	Analysis of MMP-7, -8, -9

- preparation of wash buffer: 135 mL deionized water + 15 mL wash buffer 10X
- preparation of reading buffer: 45 mL deionized water + 5 mL reading buffer 10X
- preparation of the lyophilized standard: 250 µL standard diluent + lyophilized standard (vortex for 15 seconds), incubation on ice for 10 min
  - serial dilution preparation:
  - standard = C7, labelling of tubes C7- C0
  - addition of 160 µL of standard diluent to C6-C1, preparation of 1:3 dilution transferring 80µl of the standard

The entire assay was performed on a filter-plate.

- preparation of filter plate: wash with 100 µL wash buffer, centrifugation at 300 rpm for 30 seconds, flow-through discarded
- addition of 45 µL bead suspension to each well, centrifugation at 300 rpm for 30 seconds, flow-through discarded
- addition of 30 µL assay buffer to each sample well
- addition of 15 µL of samples (no dilution!) to each sample well
- addition of 45 µL standard to each standard well
- sealing the plate with aluminium foil
- overnight incubation on a plate shaker (500 rpm at 4 °C)
- washing the wells 3 times with 100 µL wash buffer and centrifugation at 300 rpm for 30 seconds, flow-through discarded after each washing step
- addition of 25 µL of biotinylated antibody working solution to each well
- sealing the plate with aluminium foil
- shaking at 500 rpm for 1 hour at room temperature
- washing the wells 3 times with 100 µL wash buffer and centrifugation at 300 rpm for 30 seconds, flow-through discarded
- addition of 25 µL of SA-PE to each well and sealing the plate with aluminium foil

- shaking at 500 rpm for 30 min at room temperature
- washing the wells twice with 100 µL wash buffer, centrifugation at 300 rpm for 30 seconds, flow-through discarded after each washing step
- addition of 150 µL reading buffer and covering the plate with a plate seal
- reading samples on flow cytometer with 100 events per cytokine, thus 300 events

SA-PE: Streptavidin-Phycoerythrin

Table S3. Quantitative evaluation of pro-inflammatory cytokines when all groups were pooled and differentiated for the single interventional groups: guttapercha (GP), Biodentine (BD), Clearfil Protect Bond (PB), Clearfil SE Bond 2 (SE) (median, maximum, minimum; concentration, pg/mL).

	Median (Min – Max), pg/mL								
	IL-1β *visit 1*	IL-1β *visit 2*	$p^{\dagger}$	IL-6 *visit 1*	IL-6 *visit 2*	$p^{\dagger}$	CRP *visit 1*	CRP *visit 2*	$p^{\dagger}$
all groups	107.35 (0.96 – 1728.60)	2.27 (0.00 – 213.59)	**<0.001**	3.81 (0 – 58.54)	0.00 (0.00 – 4.33)	**<0.001**	304.89 (0.00 – 20626.52)	67.76 (0.00 – 3628.34)	**<0.001**
GP	111.10 (0.96 – 1728.60)	8.45 (0.00 – 213.59)	**0.008**	4.71 (0.00 – 41.88)	0.00 (0.00 – 4.33)	**0.028**	377.67 (0.00 – 12752.43)	85.87 (0.00 – 1287.02)	**0.041**
BD	115.98 (1.32 – 1456.96)	2.14 (0 – 97.14)	**0.007**	3.81 (0.00 – 14.31)	0.00 (0.00 – 2.21)	**0.012**	1018.74 (15.96 – 20626.52)	98.01 (18.05 – 3628.34)	**0.047**
PB	103.59 (3.06 – 496.85)	1.08 (0.00 – 12,63)	**0.018**	0.00 (0.00 – 43.90)	0.00 (0.00 – 0.00)	0.109	219.21 (18.05 – 1019.85)	67.76 (0.00 – 438.42)	0.091
SE	66.51 (5.95 – 237.22)	0.00 (0.00 – 21.03)	**0.028**	6.49 (0.00 – 58.54)	0.00 (0.00 – 0.00)	0.068	131.13 (44.68 – 788.36)	39.90 (0.00 – 273.4)	0.091

†Wilcoxon test

Table S4. Quantitative evaluation of matrix metalloproteinases when all groups were pooled and differentiated for the single interventional groups: guttapercha (GP), Biodentine (BD), Clearfil Protect Bond (PB), Clearfil SE Bond 2 (SE) (median, maximum, minimum; concentration, pg/mL).

	Median (Min – Max), pg/mL								
	MMP-7 *visit 1*	MMP-7 *visit 2*	$p^{\dagger}$	MMP-8 *visit 1*	MMP-8 *visit 2*	$p^{\dagger}$	MMP-9 *visit 1*	MMP-9 *visit 2*	$p^{\dagger}$
all groups	141.42 (52.83 – 547.36)	155.56 (60.61 – 653.22)	0.122	2481,63 (72.67 – 29168.48)	7805.40 (26.46 – 146831.88)	**0.016**	822.15 (46.79 – 108743.19)	1363.22 (43.71 – 176680.20)	0.264
GP	141.42 (78.08 – 435.72)	307.02 (73.18 – 653.22)	0.214	3694.43 (374.34 – 17979.70)	8488.92 (270.48 – 146831.88)	0.173	413.46 (68.62 – 108743.19)	818.44 (49.89 – 176680.20)	0.314
BD	123.88 (52.83 – 247.92)	126.13 (60.61 – 291.18)	0.263	641.09 (72.67 – 13570.06)	7495.00 (26.46 – 53568.46)	0.161	648.67 (46.79 – 3988.13)	285.14 (43.71 – 31259.98)	0.327
PB	195.11 (75.64 – 519.7)	200.84 (136.42 – 515.07)	0.612	3046.79 (97.41 – 17278.35)	12535.42 (113.24 – 52973.52)	0.176	3526.33 (78.05 – 30313.80)	6923.04 (193.92 – 35758.05)	0.499
SE	148.79 (68.21 – 547.36)	156.15 (99.37 – 539.64)	0.735	1989.71 (233.24 – 29168.48)	3192.24 (208.54 – 25914.02)	0.866	1828.00 (193.92 – 29148.36)	1291.75 (100.11 – 14007.14)	0.499

†Wilcoxon test

Table S5. Quantitative evaluation of tissue inhibitor of metalloproteinases when all groups were pooled and differentiated for the single interventional groups: guttapercha (GP), Biodentine (BD), Clearfil Protect Bond (PB), Clearfil SE Bond 2 (SE) (median, maximum, minimum, pg/mL).

	Median (Min – Max), pg/mL					
	TIMP-1 *visit 1*	TIMP-1 *visit 2*	$p^{\dagger}$	TIMP-2 *visit 1*	TIMP-2 *visit 2*	$p^{\dagger}$
all groups	198.6 (0.00 – 1011.16)	245.80 (0.00 – 683.49)	0.688	86.04 (0.00 – 555.35)	0.00 (0.00 – 307.63)	**< 0.001**
GP	267.04 (0.00 – 961.35)	205.22 (0.00 – 683.49)	0.799	70.29 (0.00 – 466.35)	0.00 (0.00 – 103.44)	**0.036**
BD	198.60 (0.00 – 615.66)	160.32 (0.00 – 580.35)	0.799	141.05 (0.00 – 555.35)	0.00 (0.00 – 307.63)	**0.038**
PB	155.99 (0.00 – 823.05)	462.96 (133.52 – 556.26)	0.237	70.29 (0.00 – 175.48)	0.00 (0.00 – 68.16)	0.080
SE	207.18 (0.00 – 1011.16)	329.18 (0.00 – 568.38)	0.463	68.31 (0.00 – 191.92)	0.00 (0.00 – 28.49)	**0.046**

† Wilcoxon test