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Supplemental information

Cross-modal contrastive learning

for unified placenta analysis using photographs

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Supplemental Methods

In this section, we provide additional results to support the analysis of PlacentaCLIP.

Including Stage 1 as Negative Samples in MIR and FIR

Table S1 presents the performance of MIR and FIR when stage 1 is included as a negative case. In the main text, stage 1 is excluded from the metric computation. We observe that including stage 1 as negative increases the standard deviation of the model's results, while the mean performance remains largely unchanged. This outcome is expected, as stage 1 is more challenging to identify.

Analysis of Variance for Combined Factors of Introduced Artificial Corruptions

We conducted an Analysis of Variance (ANOVA) analysis considering up to three combined effects, applied in a fixed order of corruption. These combined effect results encompass 175 comparisons for each task. Given the large size of the table containing these comparisons, it is provided separately in the Supplemental Information, allowing readers to filter. Only the significant variables with a P-value < 0.05 are shown here. Calculating all interactions for the 10 proposed corruptions in all possible orders would result in 10! = 3,628,800 comparisons, which would be impractical. All analyses are conducted on PlacentaCLIP, in contrast to the more robust PlacentaCLIP+, to better reveal the differences in robustness.

Overall, the application of individual artifacts consistently impacts model performance, but the additional application of artifacts rarely affects performance (6.1% to 18.2% of the time). The model demonstrates the highest robustness in the sepsis classification task, with only 6.1% of the combined variables (Table S6) showing a statistically significant effect on performance. Conversely, the model exhibits the least robustness in the meconium classification task, where 18.2% of the combined variables (Table S2) show a statistically significant effect. Performance in the meconium classification task (Table S2) is most impacted by the additional application of color-based artifacts, such as saturation. In contrast, performance in other tasks (Table S3, Table S4, Table S5, and Table S6) is less affected by color-based artifacts. The performance in chorioamnionitis classification is less affected by the additional application of brightness artifacts compared to FIR (Table S4) and MIR (Table S5).

Due to the complexity of analyzing combined effects, more insights are drawn from direct performance comparisons discussed in the main text.

Effect of Class Distribution on Model Performance Across Different Demographic Groups

We conducted an additional analysis on the percentage of positive samples for each placenta feature and clinical outcome across different races in the internal validation set to identify any biases that might contribute to the model performing better on the 'Unknown' group than on the 'White' group. From Table S7, we observe that the 'Unknown' group has a significantly higher positive sample rate than the 'White' group for sepsis. Since our model performs best on the sepsis classification task, this disparity in class distribution is a contributing factor to the performance difference.

Table S1: The performance of PlacentCLIP on MIR and FIR with and without discarding stage 1

	mAP	STD	AUC	STD
FIR w/o stage 1	80.17	1.92	84.97	0.77
FIR w/ stage 1	78.47	4.81	82.72	2.71
MIR w/o stage 1	77.84	0.98	77.89	0.42
MIR w/ stage 1	79.11	2.77	79.97	3.35

The standard deviation increases when stage 1 is included as negative samples but the mean performance did not change too much. STD: standard deviation. mAP: mean average precision. AUC: area under the receiver operating characteristic curve.

Variables	SS	DoF	F	P-value
Blood	1064.381	1.000	351.344	0.000
Glare	179.239	1.000	59.165	0.000
Shadow	2238.017	1.000	738.753	0.000
Defocus blur	15374.586	1.000	5075.035	0.000
Motion blur	3786.043	1.000	1249.744	0.000
Zoom blur	704.864	1.000	232.670	0.000
Contrast	487.091	1.000	160.785	0.000
Brightness	2102.790	1.000	694.115	0.000
Saturation	1250.147	1.000	412.664	0.000
JPEG	7500.377	1.000	2475.818	0.000
Blood : Shadow	15.125	1.000	4.993	0.026
Blood : Defocus blur	13.441	1.000	4.437	0.036
Blood : Motion blur	14.585	1.000	4.815	0.029
Blood : Saturation	35.000	1.000	11.553	0.001
Blood : JPEG	62.768	1.000	20.719	0.000
Glare : Shadow	13.714	1.000	4.527	0.034
Glare : Defocus blur	45.330	1.000	14.963	0.000
Glare : Motion blur	56.777	1.000	18.742	0.000
Glare : Zoom blur	12.141	1.000	4.008	0.046
Glare : Brightness	20.076	1.000	6.627	0.010
Glare : JPEG	30.888	1.000	10.196	0.001
Shadow : Zoom blur	16.664	1.000	5.501	0.019
Shadow : Contrast	47.170	1.000	15.570	0.000
Shadow : Brightness	170.366	1.000	56.236	0.000
Shadow : JPEG	38.234	1.000	12.621	0.000
Defocus blur : Motion blur	386.506	1.000	127.583	0.000
Defocus blur : Zoom blur	50.099	1.000	16.537	0.000
Defocus blur : Contrast	21.960	1.000	7.249	0.007
Defocus blur : JPEG	186.820	1.000	61.668	0.000
Motion blur : JPEG	83.677	1.000	27.621	0.000
Zoom blur : Saturation	12.841	1.000	4.239	0.040
Contrast : Brightness	13.016	1.000	4.297	0.039
Blood : Defocus blur : Brightness	14.621	1.000	4.826	0.028
Blood : Defocus blur : JPEG	38.493	1.000	12.706	0.000
Blood : Motion blur : JPEG	12.135	1.000	4.006	0.046
Blood : Zoom blur : JPEG	11.805	1.000	3.897	0.049
Glare : Shadow : Saturation	13.342	1.000	4.404	0.036
Glare : Motion blur : JPEG	15.246	1.000	5.032	0.025
Glare : Saturation : JPEG	13.182	1.000	4.351	0.037
Shadow : Defocus blur : Brightness	43.748	1.000	14.441	0.000

Table S2: Significant variables in the combined ANOVA analysis for the effects of synthetic artifacts on the performance of meconium

Overall, the individual application of artifacts consistently produces a significant effect on model performance. However, the additional application of artifacts less frequently affects model performance (18.2% of the time). The performance of meconium is particularly affected by color artifacts such as brightness, contrast, and saturation. JPEG compression also causes an additional performance drop. DoF: degree of freedom. SS: sum of squares. F: F-statistics.

Variables	SS	DoF	F	P-value
Blood	1373.483	1.000	236.825	0.000
Glare	601.677	1.000	103.745	0.000
Shadow	24.980	1.000	4.307	0.038
Defocus blur	6184.953	1.000	1066.450	0.000
Motion blur	2814.474	1.000	485.290	0.000
Zoom blur	710.379	1.000	122.488	0.000
Contrast	229.095	1.000	39.502	0.000
Brightness	1970.601	1.000	339.784	0.000
Saturation	109.970	1.000	18.962	0.000
JPEG	3944.526	1.000	680.141	0.000
Glare : Defocus blur	268.935	1.000	46.372	0.000
Glare : Motion blur	59.448	1.000	10.250	0.001
Glare : Zoom blur	24.644	1.000	4.249	0.040
Glare : JPEG	33.307	1.000	5.743	0.017
Shadow : Defocus blur	45.996	1.000	7.931	0.005
Shadow : JPEG	55.077	1.000	9.497	0.002
Defocus blur : Motion blur	138.841	1.000	23.940	0.000
Defocus blur : Zoom blur	27.204	1.000	4.691	0.031
Defocus blur : JPEG	209.837	1.000	36.182	0.000
Motion blur : Zoom blur	39.032	1.000	6.730	0.010
Motion blur : JPEG	22.394	1.000	3.861	0.050
Blood : Shadow : Motion blur	25.051	1.000	4.319	0.038
Blood : Defocus blur : JPEG	22.576	1.000	3.893	0.049
Glare : Defocus blur : Contrast	23.719	1.000	4.090	0.044

Table S3: Significant variables in the combined ANOVA analysis for the effects of synthetic artifacts on the performance of chorioamnionitis

Overall, the individual application of artifacts always produces a significant effect on model performance. However, the additional application of artifacts less frequently affects model performance (8.5% of the time). The performance of chorioamnionitis tends to be affected by additional blur or JPEG compression. DoF: degree of freedom. SS: sum of squares. F: F-statistics.

Variables	SS	DoF	F	P-value
Blood	1614.241	1.000	333.964	0.000
Glare	535.509	1.000	110.789	0.000
Shadow	1150.898	1.000	238.105	0.000
Defocus blur	11910.097	1.000	2464.035	0.000
Motion blur	3292.658	1.000	681.206	0.000
Zoom blur	968.583	1.000	200.386	0.000
Contrast	350.373	1.000	72.487	0.000
Brightness	2976.847	1.000	615.869	0.000
Saturation	402.393	1.000	83.250	0.000
JPEG	7668.328	1.000	1586.471	0.000
Blood : Defocus blur	71.453	1.000	14.783	0.000
Blood : Brightness	48.186	1.000	9.969	0.002
Glare : Defocus blur	225.605	1.000	46.675	0.000
Glare : Motion blur	116.425	1.000	24.087	0.000
Glare : Zoom blur	32.331	1.000	6.689	0.010
Glare : JPEG	21.182	1.000	4.382	0.037
Shadow : Brightness	62.141	1.000	12.856	0.000
Shadow : Saturation	22.735	1.000	4.704	0.030
Defocus blur : Motion blur	56.735	1.000	11.738	0.001
Defocus blur : Brightness	19.432	1.000	4.020	0.045
Defocus blur : JPEG	20.588	1.000	4.259	0.039
Defocus blur : Motion blur : JPEG	30.999	1.000	6.413	0.012
Defocus blur : Brightness : JPEG	19.218	1.000	3.976	0.047

Table S4: Significant variables in the combined ANOVA analysis for the effects of synthetic artifacts on the performance of FIR

Overall, the individual application of artifacts always produces a significant effect on model performance. However, the additional application of artifacts less frequently affects model performance (7.9% of the time). The performance of FIR tends to be affected by additional blur or JPEG compression. DoF: degree of freedom. SS: sum of squares. F: F-statistics.

Variables	SS	DoF	F	P-value
Blood	2165.961	1.000	451.340	0.000
Glare	876.761	1.000	182.698	0.000
Shadow	392.768	1.000	81.844	0.000
Defocus blur	12153.796	1.000	2532.589	0.000
Motion blur	3499.102	1.000	729.138	0.000
Zoom blur	727.716	1.000	151.640	0.000
Contrast	119.325	1.000	24.865	0.000
Brightness	1610.976	1.000	335.693	0.000
Saturation	212.483	1.000	44.277	0.000
JPEG	8092.322	1.000	1686.266	0.000
Blood : Motion blur	19.020	1.000	3.963	0.047
Blood : JPEG	40.062	1.000	8.348	0.004
Glare : Shadow	37.054	1.000	7.721	0.006
Glare : Defocus blur	416.777	1.000	86.847	0.000
Glare : Motion blur	140.896	1.000	29.360	0.000
Glare : Zoom blur	28.145	1.000	5.865	0.016
Glare : Saturation	19.681	1.000	4.101	0.043
Shadow : Contrast	40.752	1.000	8.492	0.004
Shadow : Brightness	108.975	1.000	22.708	0.000
Shadow : JPEG	62.753	1.000	13.076	0.000
Defocus blur : Motion blur	201.530	1.000	41.995	0.000
Defocus blur : Zoom blur	26.709	1.000	5.566	0.019
Defocus blur : Brightness	25.252	1.000	5.262	0.022
Defocus blur : JPEG	628.988	1.000	131.067	0.000
Motion blur : JPEG	91.318	1.000	19.029	0.000
Defocus blur : Motion blur : Zoom blur	28.910	1.000	6.024	0.014

Table S5: Significant variables in the combined ANOVA analysis for the effects of synthetic artifacts on the performance of MIR

Overall, the individual application of artifacts always produces a significant effect on model performance, but additional applications of artifacts affect model performance less frequently (9.7% of the time). The performance of MIR tends to be affected by additional blur or JPEG compression. DoF: degree of freedom. SS: sum of squares. F: F-statistics.

Variables	SS	DoF	F	P-value
Blood	617.963	1.000	101.651	0.000
Glare	886.889	1.000	145.887	0.000
Shadow	1431.548	1.000	235.480	0.000
Defocus blur	3247.595	1.000	534.207	0.000
Motion blur	813.714	1.000	133.850	0.000
Zoom blur	217.950	1.000	35.851	0.000
Contrast	388.370	1.000	63.884	0.000
Brightness	1512.863	1.000	248.855	0.000
Saturation	170.926	1.000	28.116	0.000
JPEG	576.612	1.000	94.849	0.000
Blood : Defocus blur	27.230	1.000	4.479	0.035
Glare : Defocus blur	145.333	1.000	23.906	0.000
Glare : Motion blur	41.600	1.000	6.843	0.009
Glare : JPEG	51.284	1.000	8.436	0.004
Shadow : JPEG	59.986	1.000	9.867	0.002
Defocus blur : Motion blur	79.073	1.000	13.007	0.000
Defocus blur : Brightness	50.342	1.000	8.281	0.004
Saturation : JPEG	27.838	1.000	4.579	0.033
Shadow : Defocus blur : Brightness	28.600	1.000	4.705	0.030
Defocus blur : Motion blur : Brightness	28.522	1.000	4.692	0.031

Table S6: Significant variables in the combined ANOVA analysis for the effects of synthetic artifacts on the performance of sepsis

Overall, the individual application of artifacts always produces a significant effect on model performance, but additional applications of artifacts affect model performance less frequently (6.1% of the time). The performance of sepsis tends to be affected by additional blur or JPEG compression. DoF: degree of freedom. SS: sum of squares. F: F-statistics.

Table S7: The percentage of positive samples for each placenta feature and clinical outcome across different races in the internal validation set

	Meconium	Chorioamnionitis	FIR	MIR	Sepsis
Asian	50.00%	57.14%	39.39%	61.04%	20.00%
Black or African American	45.35%	52.31%	50.00%	53.47%	18.18%
Other	49.46%	65.57%	52.00%	58.59%	23.53%
Unknown	40.43%	57.89%	39.13%	59.70%	25.00%
White	46.34%	39.66%	41.30%	49.45%	7.02%

FIR: fetal inflammatory response; MIR: maternal inflammatory response.

Data S1. Photo-taking procedure at Mbarara Regional Referral Hospital

Photographing the placenta – **FETAL** surface

- Tuck membranes under disc so they are not showing
- Lay cord off of placenta from the shortest edge start by laying it straight off the closest edge of the placenta
- Arrange the cord straight/curved around the disc (NOT curled up); don't let cord touch the disc or touch itself
- Wipe the placental surface to reduce glare (make sure there is no light reflecting on the placenta's shiny surface)
- Wipe blood and clots off disc and cord
- Wipe blood off blue board
- Include entire ruler in photo (bottom)
- Include ID in photo (bottom right)



Take fetal side photo – check that image is **in focus** with **no glare** and **no shadows** – take a second photo to be sure Take additional, close-up photograph(s) of any visible lesions

Photographing the placenta – MATERNAL surface

- Turn the disc over
- Center disc and tuck membranes and cord under disc (NO cord segments should be visible)
- Wipe blood and clots off maternal disc surface
- Wipe blood off of blue background.
- Include all fragments of the placenta if disc is not whole
- Ensure ruler and ID number are still in place in the photo and are not touching disc or cord



Take maternal side photo – check that image is **in focus** with **no glare** and **no shadows** – take a second photo to be sure Take additional, close-up photograph(s) of any visible lesions

CHECK your photos



Press the <u>left</u> side of the large round button to look at the previous photo – Press the <u>right</u> side of the large round button to look at the next photo –



CHECK to be sure:

- 1. The photo is clear, in focus, and not blurry
- 2. All portions of the placenta are entirely contained in the photo
- 3. These are **NOT** in the photo:
 - a. Non-adherent blood clots
 - b. Blood on the disc of blue background
 - c. Hands
 - d. Feet
 - e. Clothing
 - f. Tools
 - g. Containers
 - h. Wipes or paper towels
 - i. Blood stains
 - j. Motion
 - k. Glare (reflection use gauze to dry wet areas)
 - I. Uneven lighting, shadows
- 3. The placenta and cord are not be touching
- 4. The cord is not touching itself
- 5. The entire ruler is visible in the photo
- 6. There is space between the items blue background is visible in-between each item

TAKE MORE PHOTOGRAPHS if you see any of these problems, or if you're not sure (it is easier to delete them later)