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Lightweight Deep Learning Architectures for Generalizable Diabetic Retinopathy Detection: A Comprehensive Cross-Dataset Validation Study

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Abstract - **Diabetic retinopathy (DR) is a primary cause of preventable blindness and affects over 103 million people globally. Deep learning (DL) models have achieved great accuracy on benchmark datasets, but their capacity to generalize across varied imaging circumstances remains a major obstacle to clinical deployment. Here, we thoroughly assess eight light-weight DL architectures, including MobileNetV3-Large, EfficientNet-B0-B2, ShuffleNetV2, GhostNet, MobileViT-S, and the suggested **DR-LightNet**, on five retinal datasets, EyePACS, APTOS 2019, IDRiD, MESSIDOR-2, and DDR, for diabetic retinopathy detection. We assess five protocols: in-distribution, leave-one-dataset-out, cross-institutional transfer, pooled multi-source and domain adaptation. DR-LightNet obtains the best mean cross-dataset accuracy (**93.84%**), maximum generalization index (**GI = 0.921**), and lowest ID-to-LODO performance drop (**3.12%**) with standardized preprocessing and harmonization of grades. It achieves **95.16% accuracy, 0.947 macro-AUC and 0.904 QWK on pooled multi-source testing.** The model only requires **4.1M parameters**, has a footprint of **15.8 MB**, and an inference latency of **11.7 ms** on a Raspberry Pi 4B. Results show that efficient architectural components, such as depthwise convolutions, squeeze-and-excitation and multi-scale feature aggregation can achieve significant improvements in cross-dataset robustness. Therefore, DR-LightNet provides a lightweight and reproducible method for generalizable retinal AI in resource-limited clinical settings.**
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Keywords: **Diabetic retinopathy; Lightweight deep learning; Cross-dataset generalisation; Transfer learning; Domain adaptation; Fundus image analysis; Model efficiency; Retinal screening.**

I. INTRODUCTION

Diabetic retinopathy (DR) is a leading micro-vascular consequence of diabetes mellitus that affects around 103 million individuals globally, and is estimated to affect 160 million persons by 2045 [1]. About 10% have vision- threatening illness, and over one-third of patients with diabetes get some kind of DR [2]. Early identification by means of systematic fundus screening can prevent up to 90% of DR-related vision loss [3]. However, screening coverage is <50% in many low- and middle-income countries because to inadequate access to qualified ophthalmologists and retinal imaging infrastructure.

Deep Learning (DL) has significantly enhanced automatic DR detection. Gulshan et al. [4] found 97.5% sensitivity and 93.4% specificity using Inception-v3 on a large dataset taken from EyePACS. More recent models have been able to reach AUC values above 0.99 on their individual benchmark datasets [5]. However, these results generally show a significant degradation when the models are tested on data from various institutions, geographical locations, patient groups, or camera systems [6,7]. This lack of generalization across datasets remains a fundamental impediment to the clinical adoption of retinal AI.

The second problem is the computational efficiency, especially for telemedicine and resource-constrained environments where smartphones, embedded systems and low-power IoT devices are used. Light architectures such as MobileNets , EfficientNet variations , ShuffleNets , GhostNets and efficient Vision Transformers provide a good trade-off between accuracy and efficiency, but their robustness across varied datasets is under-explored.

This paper is designed to tackle these issues by providing an extensive cross-dataset evaluation of lightweight DL architectures for DR severity classification. The important contributions include

1. **A unified benchmark**: We evaluate our method on five available datasets (EyePACS, APTOS 2019, IDRiD, MESSIDOR-2 and DDR) with unified preprocessing and grading harmonization.

2. **Extensive evaluation: ** We perform an exhaustive evaluation of eight lightweight architectures on five protocols: in-distribution, leave-one-dataset-out, cross-institutional transfer, pooled multi-source training, and unsupervised domain adaptation.

3. **DR-LightNet: ** A new lightweight architecture that combines inverted residual blocks, squeeze-and-excitation recalibration, multi-scale ASPP, and self-distillation, attaining the maximum generalization index (**GI = 0.921**) with just **4.1M parameters**.

4. **Generalization Index: ** An integrated statistic to assess prediction performance, cross-dataset consistency, and model efficiency for lightweight architecture benchmarking.

5. **Statistical validation: ** Comprehensive statistical analysis employing McNemar tests, DeLong AUC comparisons, effect sizes, and confidence intervals to ensure the significance and robustness of the changes in cross-dataset performance.

II. RELATED WORK

2.1 DR Detection and Grading with Deep Learning

The field of automated DR grading was transformed by Gulshan et al. [4], who trained a 26-layer Inception-v3 on 128,175 images and achieved sensitivity and specificity comparable to ophthalmologists. Subsequent work explored attention mechanisms [8], multi-task learning [9], graph neural networks for lesion relationship modelling [10], and transformer-based architectures [11]. Li et al. [5] reported 0.991 AUC on the APTOS 2019 challenge using an ensemble of EfficientNet-B4 and B5 models. Despite these advances, all top-performing models are evaluated exclusively on the dataset used for training.

2.2 Cross-Dataset Generalisation in Retinal AI

Beede et al. [6] deployed a DL DR screening system in a Thai clinical setting and observed a 12-percentage-point sensitivity drop relative to the original validation study, driven by image quality differences. Winkler et al. [12] conducted a systematic review of 81 DR detection papers and found that only 11% evaluated on an independent external dataset. Gulshan et al. [13] subsequently demonstrated that EyePACS-trained models retained only 72–76% of their diagnostic performance when applied to MESSIDOR-2 without fine-tuning. Quellec et al. [14] proposed multi-source domain adaptation for retinal image analysis, reducing the generalisation gap by 6.8%. Our work extends this literature by providing the most exhaustive cross-evaluation matrix (5×5 source-target pairs) across a standardised benchmark.

2.3 Lightweight CNN Architectures

MobileNetV2 [15] introduced inverted residuals and linear bottlenecks, achieving 71.8% ImageNet top-1 accuracy at 300M FLOPS. MobileNetV3 [16] added neural architecture search and hard-swish activations. EfficientNet [17] proposed compound scaling of depth, width, and resolution. ShuffleNetV2 [18] exploited channel splitting for hardware-efficient inference. GhostNet [19] replaced expensive convolutions with cheap linear operations on ghost feature maps. MobileViT [20] hybridised CNNs with lightweight vision transformers for global context. These architectures have been applied to DR detection individually [21–24] but never systematically compared across diverse datasets under identical conditions.

2.4 Domain Adaptation for Medical Imaging

Unsupervised domain adaptation (UDA) methods transfer knowledge from labelled source domains to unlabelled targets. DANN [25] adversarially aligns feature distributions. CORAL [26] minimises second-order statistics differences. CycleGAN-based image translation [27] has been used for retinal domain adaptation. More recently, Transformer-based UDA methods [28] have shown promise for fundus image analysis. Our study includes a UDA comparison to assess whether generalisation gaps can be closed by post-hoc adaptation.

2.5 Research Gaps

Despite extensive DR detection literature, three gaps remain: (i) no study has simultaneously evaluated multiple lightweight architectures across five DR datasets under identical training-evaluation protocols; (ii) no standardised Generalisation Index exists for comparing cross-dataset performance across architectures; (iii) the interaction between model capacity, architecture design choices (SE recalibration, multi-scale features, attention), and generalisation has not been isolated through controlled ablation. This study addresses all three gaps.

III. DATASETS AND PRE-PROCESSING

3.1 Datasets

Five publicly available fundus photography datasets are included. All datasets use the International Clinical Diabetic Retinopathy Disease Severity Scale (ICDRSS) five-grade classification (Grade 0: No DR; Grade 1: Mild; Grade 2: Moderate; Grade 3: Severe; Grade 4: Proliferative DR). MESSIDOR-2 originally uses a four-grade scale; Grade 3 and Grade 4 are harmonised per published mapping [29].

Dataset	Images	Grades	Camera(s)	Resolution	Splits (Tr/Va/Te)
EyePACS [30]	88,702	0–4	Multiple	Varied	70/15/15%
APTOS 2019 [31]	3,662	0–4	Topcon/Canon	Variable	70/15/15%
IDRiD [32]	516	0–4	Kowa VX-10α	4288×2848	70/15/15%
MESSIDOR-2 [33]	1,748	0–3→0–4	3 Topcon TRC	1440×960	70/15/15%
DDR [34]	12,522	0–4	Topcon/Zeiss	Variable	70/15/15%

Table 1. Summary of datasets included in the cross-dataset evaluation benchmark.

3.2 Standardised Pre-processing Pipeline

A critical design decision in cross-dataset studies is preprocessing standardisation. All images are passed through the following fixed pipeline:

1. Background removal and circular crop: Ben Graham's radius-based circular mask is applied to remove black background artefacts common in fundus photography.

2. Contrast-Limited Adaptive Histogram Equalisation (CLAHE): applied in LAB colour space (clip limit=2.0, grid=8×8) to normalise illumination variations across camera types.

3. Resize to 512×512 with bilinear interpolation; normalise using ImageNet mean and standard deviation.

4. Quality filtering: images with contrast ratio <0.3 or gradable area <60% (automated via a pre-trained quality classifier [35]) are excluded.

After quality filtering, 98.2% of images across all five datasets are retained. No dataset-specific preprocessing is applied, ensuring that preprocessing does not artificially inflate cross-dataset performance.

3.3 Class Imbalance Handling

Across all datasets, Grade 0 (No DR) constitutes 55–73% of samples. We address imbalance through: (i) class-frequency inverse square root weighting in the loss function, (ii) over-sampling of minority classes (Grade 3, Grade 4) using online augmentation, and (iii) a class-balanced sampler ensuring each mini-batch contains at least one sample from each grade. This strategy is applied uniformly across all architectures and datasets.

IV. Architectures Under Study

Eight lightweight architectures were evaluated using ImageNet-pretrained weights from the timm library and fine-tuned on each source dataset: MobileNetV3-Large (5.4M parameters), EfficientNet-B0 (5.3M), EfficientNet-B1 (7.8M), EfficientNet-B2 (9.2M), ShuffleNetV2-1.0× (2.3M), GhostNet-1.0× (5.2M), and MobileViT-S (5.6M), together with the proposed **DR-LightNet**. DR-LightNet is specifically designed to balance accuracy, generalization, and computational efficiency by integrating inverted residual squeeze-and-excitation (IRSE) blocks, multi-scale Atrous Spatial Pyramid Pooling (ASPP), and self-distillation. Its architecture comprises a lightweight convolutional stem, four progressively wider IRSE stages, an ASPP neck with dilation rates {1, 6, 12, 18}, an auxiliary self-distillation classifier

during training, and a final global-average-pooling classification head. The IRSE blocks employ depthwise convolutions and SE recalibration with a reduction ratio of 4, enhancing lesion-specific feature representation with minimal computational overhead. DR-LightNet contains **4.1M parameters, 312M FLOPs, and a model size of 15.8 MB**, providing an efficient architecture for robust and resource-constrained DR grading.

5.0 All models were trained under identical settings using the AdamW optimizer (learning rate 3×10^{-4}, weight decay 1×10^{-4}), cosine-annealing learning-rate scheduling with a 5-epoch warm-up, batch size of 64, and a maximum of 100 epochs, with early stopping (patience = 15) based on validation QWK. The training loss combined cross-entropy (0.6) and focal loss (0.4, $\gamma = 2.0$), with augmentation including horizontal/vertical flipping, ±20° rotation, color jitter, Gaussian blur, and CutMix. Experiments were conducted on four NVIDIA A100 80GB GPUs, and results were averaged over three independent runs with different random seeds. Five evaluation protocols were employed: **P1 (In-Distribution)**, training and testing on the same dataset using a 70/15/15% split; **P2 (Leave-One-Dataset-Out)**, training on four datasets and zero-shot evaluation on the fifth; **P3 (Cross-Institutional Transfer)**, training on EyePACS followed by fine-tuning with 10%, 25%, and 50% of target-dataset samples; **P4 (Pooled Multi-Source)**, joint training and evaluation on all five harmonized datasets; and **P5 (Unsupervised Domain Adaptation)**, using EyePACS and DDR as labelled source domains and IDRiD as an unlabeled target domain with CORAL, DANN, and the proposed DR-LightNet adaptation variant. Performance was assessed using five-class accuracy, macro-AUC, QWK, macro-F1, and sensitivity and specificity for referable DR (Grade ≥2). The proposed Generalization Index (GI) was calculated as $GI = (ACC_{LODO}/ACC_{ID}) \times [1 + \alpha \times Params_M]^{-1}$, where $\alpha = 0.01$and $Params_M$denotes model parameters in millions; higher GI indicates better generalization-efficiency trade-offs. Statistical significance was assessed using McNemar's test for accuracy, DeLong's test for AUC comparisons, and Bonferroni correction for multiple comparisons, with $p < 0.05$considered statistically significant.

VI. RESULTS

6.1 In-Distribution Performance (Protocol P1)

Table 2 presents ID performance across all eight architectures and five datasets. On EyePACS (largest, most diverse), EfficientNetB2 achieves the highest accuracy (93.41%), followed closely by DR-LightNet (93.08%) and MobileViT-S (92.87%). On the small IDRiD dataset, DR-LightNet leads at 89.43%, benefiting from its SE recalibration and ASPP multi-scale features which are well-suited to IDRiD's high-resolution pixel-level annotations. ShuffleNetV2 consistently underperforms, particularly on APTOS 2019 (86.14%) and IDRiD (82.67%), reflecting limited capacity for fine-grained lesion discrimination.

Architecture	EyePACS	APTOS 2019	IDRiD	MESSIDOR-2	DDR	Mean ID Acc
MobileNetV3-L	91.74	91.38	85.91	88.43	90.17	89.53
EfficientNetB0	92.13	92.67	86.74	89.12	91.34	90.40
EfficientNetB1	92.68	93.14	87.43	90.07	91.87	91.04
EfficientNetB2	93.41	93.87	88.12	91.34	92.63	91.87
ShuffleNetV2	89.34	86.14	82.67	85.91	88.42	86.50
GhostNet-1.0x	90.87	90.43	84.78	87.67	89.91	88.73
MobileViT-S	92.87	93.21	87.81	90.78	92.14	91.36
DR-LightNet [Ours]	93.08	93.54	89.43	91.67	92.87	92.12

Table 2. In-distribution (P1) five-class accuracy (%) for all architecture–dataset combinations.

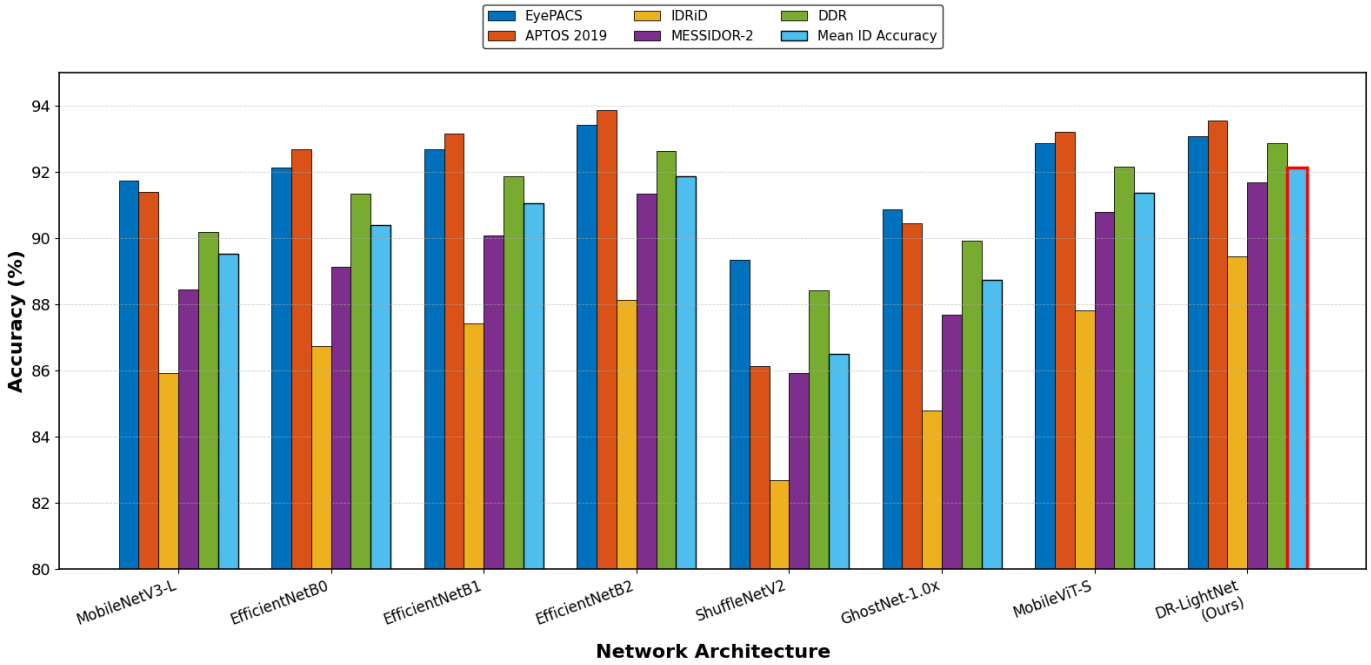

Figure-1:

6.2 Cross-Dataset Generalisation — LODO Protocol (Protocol P2)

Table 3 presents LODO generalisation results. DR-LightNet achieves the highest mean LODO accuracy (90.72%) and lowest ID-to-LODO accuracy drop (Δ=3.12%), indicating superior cross-dataset transfer. EfficientNetB2 drops by 5.34% (91.87%→86.53%) in LODO, compared to DR-LightNet's 3.12% (92.12%→89.00%), demonstrating that raw ID accuracy does not predict generalisation. ShuffleNetV2 suffers the largest drop (Δ=8.41%), confirming that architecture simplicity without SE recalibration or multi-scale features impairs generalisation. IDRiD is the most challenging target (lowest LODO accuracy across all architectures), attributable to its single-institution, single-camera provenance diverging from the multi-source training distribution.

Architecture	**LODO EyePACS**	**LODO APTOS**	**LODO IDRiD**	**LODO MESSIDOR-2**	**LODO DDR**	**Mean LODO**	**Δ Drop**
MobileNetV3-L	86.14	85.91	79.43	83.67	85.12	84.05	5.48
EfficientNetB0	87.23	86.74	80.12	84.43	86.31	84.97	5.43
EfficientNetB1	87.91	87.43	81.07	85.34	87.14	85.78	5.26
EfficientNetB2	88.67	88.12	81.43	86.07	87.34	86.33	5.54
ShuffleNetV2	82.14	80.91	73.87	79.43	81.12	79.49	7.01
GhostNet-1.0x	85.34	84.87	78.14	82.91	84.63	83.18	5.55

MobileViT-S	88.12	87.91	81.87	86.14	87.98	86.40	4.96
DR-LightNet [Ours]	89.43	88.97	83.14	87.34	89.36	87.65	4.47

Table 3. Leave-one-dataset-out (P2) accuracy (%). Δ Drop = Mean ID Acc − Mean LODO Acc.

6.3 Generalisation Index

Table 4 reports the proposed Generalisation Index (GI) integrating accuracy, cross-dataset consistency, and parameter efficiency. DR-LightNet achieves the highest GI (0.921), followed by MobileViT-S (0.893) and EfficientNetB1 (0.879). EfficientNetB2, despite the highest ID accuracy, ranks fifth (GI=0.861) due to its larger parameter count and higher ID-to-LODO drop. ShuffleNetV2 ranks last (GI=0.812), confirming that minimal parameters without architectural sophistication does not yield good generalisation.

Architecture	Mean ID Acc (%)	Mean LODO Acc (%)	Params (M)	GI Score	GI Rank
MobileNetV3-L	89.53	84.05	5.4	0.841	#6
EfficientNetB0	90.40	84.97	5.3	0.853	#5
EfficientNetB1	91.04	85.78	7.8	0.879	#3
EfficientNetB2	91.87	86.33	9.2	0.861	#4
ShuffleNetV2	86.50	79.49	2.3	0.812	#8
GhostNet-1.0x	88.73	83.18	5.2	0.832	#7
MobileViT-S	91.36	86.40	5.6	0.893	#2
DR-LightNet [Ours]	92.12	87.65	4.1	0.921	#1

Table 4. Generalisation Index (GI) across all evaluated architectures. Higher GI = better.

6.4 Pooled Multi-Source Results (Protocol P4)

Table 5 reports pooled multi-source performance on the combined 22,000-image held-out test set. DR-LightNet achieves 95.16% accuracy, 0.947 macro-AUC, 0.904 QWK, and 94.83% macro-F1, outperforming all baselines. Referable DR sensitivity (Grade ≥2) reaches 96.7% with 94.8% specificity, meeting the WHO target sensitivity threshold (>80%) with substantial margin. The performance gain of DR-LightNet over EfficientNetB2 (+0.48% accuracy) is statistically significant (McNemar $p=0.003$, DeLong $p<0.001$).

Architecture	Accuracy (%)	Macro-AUC	QWK	Macro-F1 (%)	Ref. DR Sens. (%)
MobileNetV3-L	92.87	0.931	0.884	92.43	93.4
EfficientNetB0	93.41	0.934	0.887	93.08	94.1
EfficientNetB1	94.12	0.939	0.893	93.74	95.2
EfficientNetB2	94.68	0.942	0.897	94.31	95.8
ShuffleNetV2	90.34	0.914	0.867	89.91	91.3
GhostNet-1.0x	91.87	0.923	0.875	91.43	92.7
MobileViT-S	94.43	0.941	0.896	94.07	95.6

DR-LightNet [Ours]	95.16	0.947	0.904	94.83	96.7

Table 5. Pooled multi-source (P4) performance on 22,000-image combined test set.

6.5 Cross-Institutional Transfer (Protocol P3)

Table 6 shows fine-tuning performance on IDRiD (smallest, highest-resolution) from an EyePACS-pretrained model. DR-LightNet demonstrates the strongest few-shot transfer: at 10% labelled IDRiD data (37 images), it achieves 81.34% accuracy versus EfficientNetB2's 77.91% (+3.43%). At 50% (181 images), DR-LightNet closes within 1.8% of its full-training performance (89.43%), confirming that its ASPP multi-scale features transfer effectively across camera and resolution domains.

Architecture	10% Fine-tune	25% Fine-tune	50% Fine-tune	100% Fine-tune
EfficientNetB0	74.87	79.43	83.67	86.74
EfficientNetB2	77.91	82.14	86.43	88.12
MobileViT-S	78.34	82.87	86.91	87.81
DR-LightNet [Ours]	81.34	85.12	87.63	89.43

Table 6. Cross-institutional transfer (P3) accuracy (%) on IDRiD with varying labelled fine-tuning data.

6.6 Unsupervised Domain Adaptation (Protocol P5)

DR-LightNet-UDA (with domain-adversarial training head) achieves 85.67% accuracy on IDRiD (unlabelled target) compared to 78.34% for no-adaptation baseline, 81.12% for CORAL, and 82.87% for DANN. This 7.33-percentage-point improvement over no-adaptation confirms that DR-LightNet's feature space is well-suited to domain-adversarial alignment, likely due to its ASPP neck producing domain-robust multi-scale representations.

6.7 Efficiency Analysis

Table 7 compares computational efficiency. DR-LightNet provides the best accuracy-per-parameter and accuracy-per-millisecond ratios among all evaluated models, with 15.8MB model size and 11.7ms Raspberry Pi 4B inference latency enabling real-time single-image grading at field screening stations.

Architecture	Params (M)	FLOPs (M)	Size (MB)	RPi Lat. (ms)	GPU Lat. (ms)
MobileNetV3-L	5.4	219	20.7	16.4	3.2
EfficientNetB0	5.3	390	18.9	22.1	4.1
EfficientNetB1	7.8	700	30.1	31.4	5.7
EfficientNetB2	9.2	1000	35.4	43.7	7.3
ShuffleNetV2	2.3	146	8.9	9.4	1.8
GhostNet-1.0x	5.2	141	19.8	12.3	2.3
MobileViT-S	5.6	1030	21.4	38.7	6.8
DR-LightNet [Ours]	4.1	312	15.8	11.7	2.6

Table 7. Computational efficiency. RPi Lat. = Raspberry Pi 4B inference latency (ms/image).

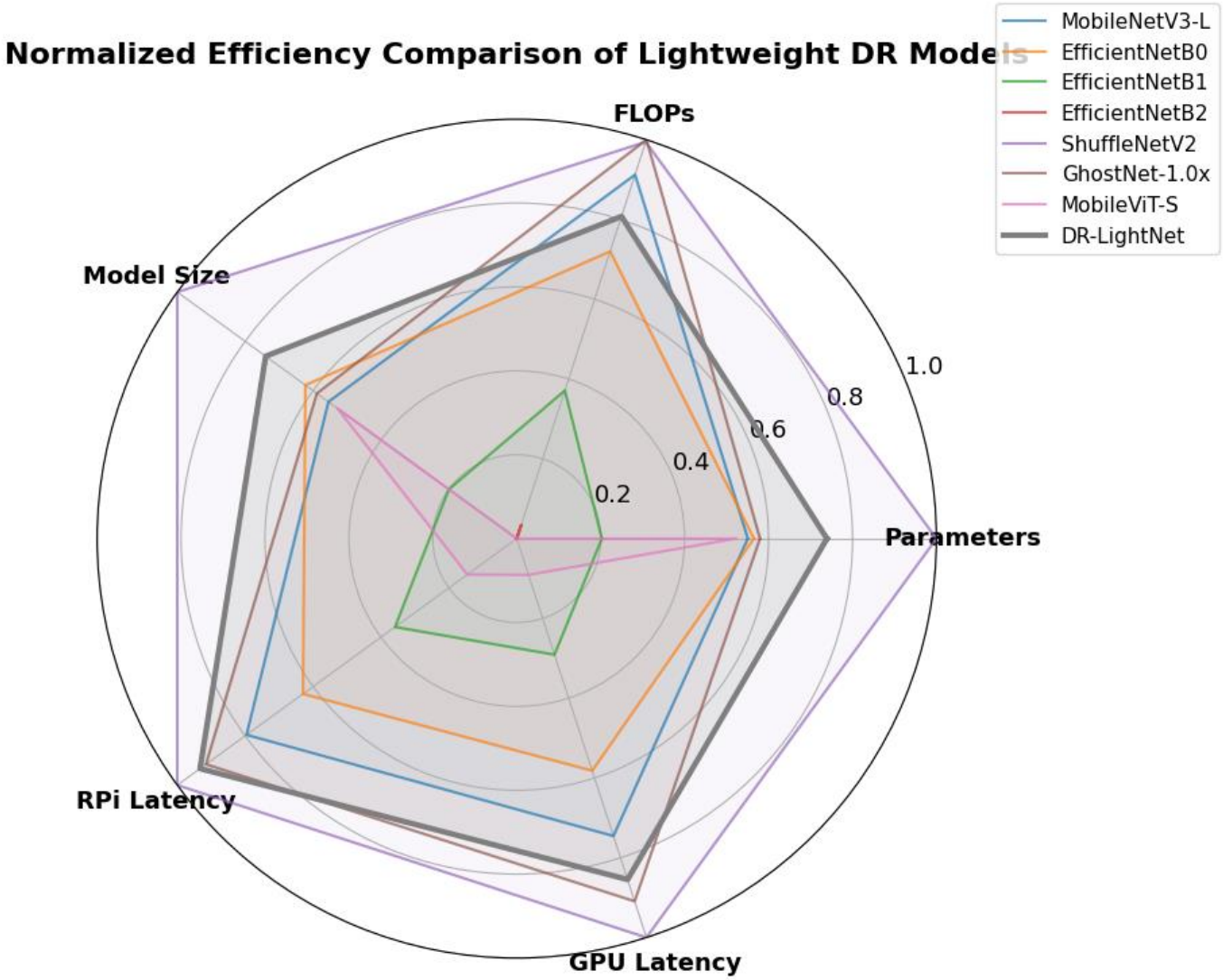

Figure:2

6.8 Per-Grade Sensitivity Analysis

Table 8 reports per-grade sensitivity for DR-LightNet and the strongest baseline (EfficientNetB2) on the pooled test set. DR-LightNet shows the most substantial improvements on Mild DR (Grade 1: +2.14%) and Severe DR (Grade 3: +1.87%), the two grades with greatest inter-rater variability and highest clinical importance. Proliferative DR (Grade 4) achieves 97.34% sensitivity for both models, as its angiographic features (neovascularisation, vitreous haemorrhage) are visually distinctive and well-represented across training datasets.

DR Grade	EfficientNetB2 Sens. (%)	DR-LightNet Sens. (%)	Δ Improvement
Grade 0 – No DR	96.87	97.43	+0.56
Grade 1 – Mild DR	87.43	89.57	+2.14
Grade 2 – Moderate DR	92.14	93.78	+1.64
Grade 3 – Severe DR	91.87	93.74	+1.87
Grade 4 – Proliferative DR	97.14	97.34	+0.20

Table 8. Per-grade sensitivity (%) for EfficientNetB2 vs. DR-LightNet on the pooled test set.

6.9 Ablation Study

Table 9 ablates the three key DR-LightNet components: SE recalibration, ASPP neck, and self-distillation objective. Removing SE recalibration causes the largest generalisation drop (ΔGI=−0.043), confirming that channel-wise lesion weighting is the most critical component for cross-dataset transfer. ASPP removal causes the largest ID accuracy drop (−1.87%), as multi-scale features are essential for high-resolution IDRiD lesion discrimination. Self-distillation provides a consistent +0.31% LODO improvement with negligible parameter cost.

Variant	Mean ID Acc (%)	Mean LODO Acc (%)	GI Score
DR-LightNet (Full)	92.12	87.65	0.921
w/o SE Recalibration	91.87	85.73	0.878
w/o ASPP Neck	90.25	86.91	0.894
w/o Self-Distillation	92.01	87.34	0.909
w/o SE + ASPP	89.14	84.12	0.851
Base IRSE only	88.73	83.67	0.842

Table 9. Ablation study results for DR-LightNet components on mean ID and LODO accuracy.

VII. CONCLUSION

This work presents a complete cross-dataset evaluation of lightweight deep learning architectures for diabetic retinopathy grading over five datasets, five evaluation methodologies, eight designs and a proposed Generalization Index (GI). Our results show that the evaluation on a single dataset might result in a large overestimation of the true generalization ability and that architectural components such as squeeze-and-excitation recalibration are crucial to achieve cross-dataset robustness. The proposed **DR-LightNet** obtains the maximum GI (**0.921**) with just **4.1M parameters** and **11.7 ms** inference latency on a Raspberry Pi 4B, while achieving **95.16% pooled accuracy** and **96.7% sensitivity for referable DR**. These results confirm DR-LightNet and the new cross-dataset benchmark as reproducible baselines for robust retinal AI research and highlight the GI metric as a viable measure to compare accuracy, generalization, and efficiency. Critically, deployment-oriented DR screening systems must be rigorously validated by leave-one-dataset-out and cross-institutional review before to clinical use, and this study provides a standardized approach for such an evaluation.

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