Physics-Guided Synthetic cNF Progression Improves Image-Based Burden Estimation for Medical Digital Twins

Alex Dils[1, 2], Christoph Sadée[1], Krish Sangani[2], Lillian Rubino[1], Alexander Ferenchick[1, 3], Varun Wadhwa[4], Anushka Poddar[5], Tobenna Onyemeh[6], Zimuzo Onah[7], Dhruv Sharma[4], Jackson Bae[8], Max Van Puyvelde[1], Carlos Romo[9], Melinda Jen[10], Nkiru Onodugo[11], Ayesha Akinkugbe[12, 13], Qinmei Xu[1], Qingtao Kong[14], Rui Yang[15], Aisha Sokunbi[16], Shaoxiong Yao[17], Haomiao Huang[18], Ifeoma Okoye[6, 11, 19], Olivier Gevaert[1], Kavita Sarin[20]

[1]Division of Computational Medicine, Department of Medicine, Stanford University; [2]University of California, Berkeley; [3]University of Pennsylvania; [4]University of California, Davis; [5]University of Maryland, College Park; [6]University of Nigeria, Nsukka, Center for Excellence for Clinical Trials; [7]University of Nigeria Teaching Hospital Ituku-Ozalla; [8]University of California, Los Angeles; [9]Johns Hopkins School of Medicine; [10]Children's Hospital of Philadelphia, Dermatology Section; [11]University of Nigeria Teaching Hospital; [12]University of Lagos; [13]Lagos University Teaching Hospital; [14]Department of Dermatology, Jinling Hospital, Affiliated Hospital of the Medical School of Nanjing University, Nanjing, China; [15]Department of Dermatology, Second Affiliated Hospital of Nanjing Medical University, Nanjing, China; [16]University of Benin Teaching Hospital; [17]Siebel School of Computing and Data Science, University of Illinois Urbana-Champaign; [18]Matter Venture Partners; [19]University of Nigeria, Nsukka; [20]Department of Dermatology, Stanford University School of Medicine

Introduction

Background. Cutaneous neurofibromas (cNF) are the most common tumor manifestation of neurofibromatosis type 1 (NF1), a condition associated with an **8–13% lifetime risk** of malignancy [1]. Tracking their progression is core to understanding disease biology, measuring treatment efficacy, and developing medical digital twins—in silico copies of a patient that evolve in tandem with them and can be used for prognosis and treatment simulation.

Despite cNF progression being inherently longitudinal and 3D, available imaging is largely cross-sectional and 2D [2-4].

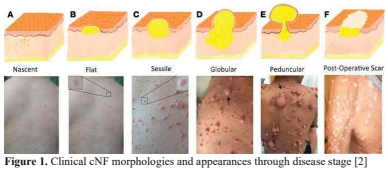

Figure 1. Clinical cNF morphologies and appearances through disease stage [2]

Mechanistic modeling can simulate lesion growth and generative AI can render those changes as realistic images, providing the longitudinal and 3D imaging needed for medical digital twin development [6–8].

Objective. Combine mechanistic modeling and generative AI to generate longitudinal and 3D data in order to improve cNF burden estimation and support future medical digital twins.

Methods

Datasets

Dataset	Images	Annotations	Train / Val / Test
Lesion	279	42,305	229 / 25 / 25
Scar	11	359	7 / 2 / 2

Table 1. Datasets and annotations used in the synthetic pipeline [9-14].

Synthetic pipeline

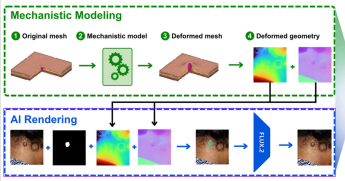

Figure 2. Morphoelastic growth [6,7] supplies geometry; FLUX.2 Klein with learned LoRA adapters [15] renders each longitudinal state.

Evaluations

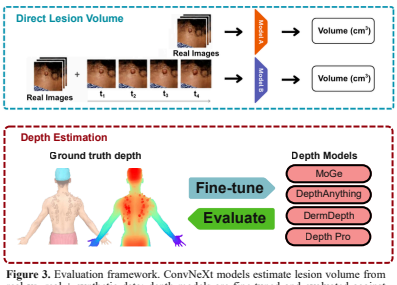

Figure 3. Evaluation framework. ConvNeXt models estimate lesion volume from real vs. real + synthetic data; depth models are fine-tuned and evaluated against ground-truth Human Scan Repository scans with grown lesions [3,16-19].

Application

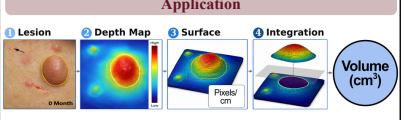

Figure 4. Volume integration by extracting lesion surface and summing volumes

Results

Pipeline results

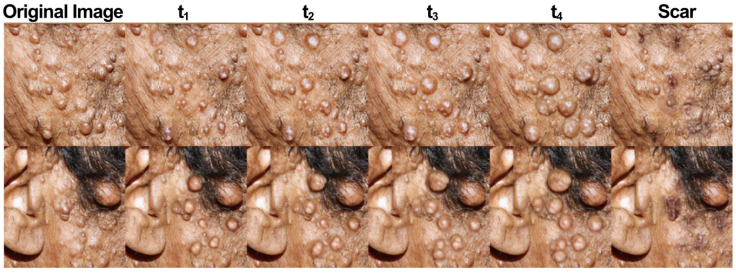

Figure 5. Four simulated growth states and a simulated post-operative scar demonstrate realistic reconstruction of longitudinal growth as well as scarring.

Synthetic data improves volume estimation

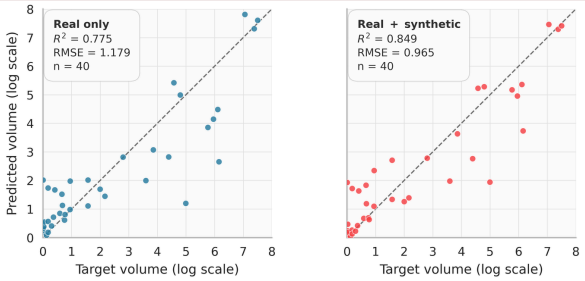

Figure 6. On 40 held-out real images, adding 4-stage synthetic growth augmentation improved volume regression.

Synthetic data improves depth models

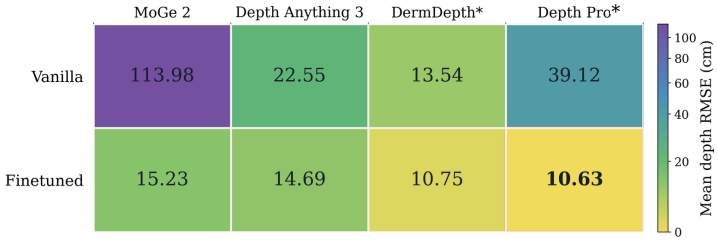

Figure 7. Depth model fine-tuning results. Lighter boxes indicate better performance.

**DermDepth and Depth Pro are not available for commercial use, so they were not used in deployment*

Deployment

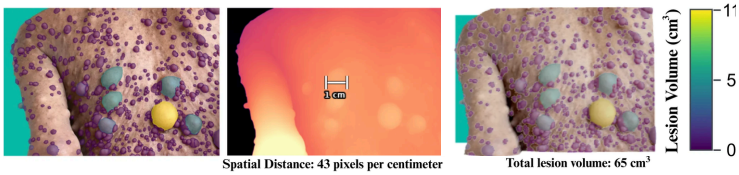

Figure 8. Calibrated scale and depth integration produce an image-level burden map. Distance model provides lesion-specific spatial distance.

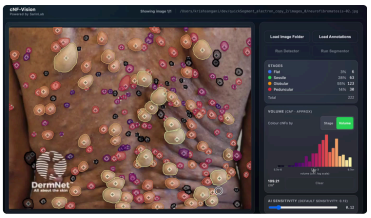

Figure 9. Screenshot of cNF-Vision with volume estimates derived from Depth Anything 3

cNF-Vision packages the pipeline into a desktop application to support cNF analysis.

- Detects individual lesions
- Classifies morphology
- Estimates per-lesion and whole-image cm³ burden
- Supports longitudinal analysis

Try early access!*

**Research use only; not clinically validated.*

Conclusion

Contributions.

Data type	Before	Generated
3D lesions	58*	**42,305**
Longitudinal sequences	1**	**279**

Table 2. Our pipeline's contribution to 3D and longitudinal data

- Developed a mechanistic + generative AI pipeline for producing realistic synthetic cNF images.
- Synthetic data improved lesion-volume estimation, increasing R^2 from **0.78 to 0.85** on the held-out test set.
- Synthetic 3D cNF data fine-tuning reduced the average RMSE from **47.30 cm to 12.83 cm**, a 72.9% reduction.
- Integrated the fine-tuned depth model into an application for automated 3D lesion measurement and longitudinal tracking.

Limitations.

- Lack of real 3D and longitudinal images to validate the simulated cNF progression and evaluations.
- Chosen patient parameters and growth function may not capture the full biology of real cNF development.

** 3D lesions not publicly available*
*** 1 longitudinal image from a paper showing three timesteps*

Future Directions

Towards medical digital twins.

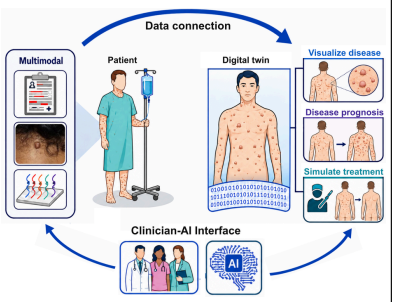

Figure 10. cNF medical digital twin workflow adapted from Sadée et al. [5]. Multimodal patient data (demographics, clinical images, skin parameters) are integrated into a patient-in-silico model to visualize disease burden, predict progression, and simulate treatment response, while clinician–AI feedback iteratively updates and refines the model.

Obtain 3D and longitudinal data.

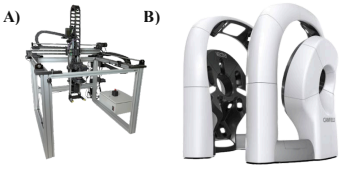

Figure 11. 3D imaging systems for skin-surface acquisition: A) OpenDerm, an open-source 3D imaging platform [20]; B) VECTRA, a commercial 3D imaging system [3,21].

Applications of depth-conditioned generative modeling.

- Integrating mechanistic knowledge and generative AI could be applied to wound healing, scar and keloid remodeling, pressure-ulcer progression, burn recovery, cutaneous tumor growth, and treatment-response simulation.

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