Supplementary Material II: Computation of Local GA Growth Rates

In this study, we computed local GA growth rates following the approach previously proposed by our group.\(^1\) In this approach, GA growth is treated as an interface propagation problem, wherein the lesion margin expands according to a specified partial differential equation. Specifically, with \(\Omega \subset \mathbb{R}^2\) the image domain, let \(G(t) \subset \Omega\) be the GA area at time \(t\) and \(\partial G(t)\) be its corresponding margin. To accommodate lesion merging (i.e., merging of margin segments of the same lesion focus and/or merging of margin segments of different lesion foci), we utilize the level set method,\(^2\) whereby the GA margin is represented as the zero level set of a higher dimensional function \(\phi\). In particular, \(G(t) = \{\phi(x, t) \leq 0\}\) and \(\partial G(t) = \{\phi(x, t) = 0\}\), with \(x \in \Omega\). The evolution of \(\phi\) is governed by the partial differential equation:

\[
\partial_t \phi(x, t) + F(\phi(x, t), \nabla \phi(x, t)) = 0
\]

(1)

where \(F\) describes the forces driving GA expansion. In this study we set:

\[
F(\phi(x, t)) = \alpha - \beta \kappa(\phi)
\]

(2)

where \(\alpha\) and \(\beta\) are positive constants and \(\kappa\) is the curvature. The same model parameter values of \(\alpha = 1\) and \(\beta = 0.75\) that were used in our previous study\(^1\) were used in the current study. As described in Moult et al.,\(^1\) the curvature term causes concave margin segments to expand more rapidly than convex segments. Let \(t_b\) be the time of the baseline visit and \(t_f\) be the time of the follow-up visit. For any given visit pair, we measure \(\partial G(t_b)\) and \(\partial G(t_f)\), which serve as our boundary conditions. In terms of the level set function, we require:

\[
\{\phi(x, t_b) = 0\} = \partial G(t_b) \quad \text{and} \quad \{\phi(x, t_f) = 0\} = \partial G(t_f)
\]

(3)

To satisfy these constraints we define the following signed distance functions:

\[
\phi_b(x) \equiv \begin{cases} 
-d(x, \partial G(t_b)) & \text{if } x \in G(t_b) \\
+d(x, \partial G(t_b)) & \text{if } x \in G^c(t_b)
\end{cases} \quad \text{and} \quad \phi_f(x) \equiv \begin{cases} 
-d(x, \partial G(t_f)) & \text{if } x \in G(t_f) \\
+d(x, \partial G(t_f)) & \text{if } x \in G^c(t_f)
\end{cases}
\]

(4)

where \(d\) is the Euclidean distance function, and \(G^c\) is the complement of \(G\). With this, we set the boundary conditions on \(\phi\) as:
\[ \phi(x, t_b) = \phi_b(x) \quad \text{and} \quad \phi(x, t_f) = \phi_f(x) \] (5)

During the evolution of \( \phi \) we ensure that the second condition of Eq. 5 is satisfied by enforcing

\[ \phi_f(x) \leq \phi(x, t) \quad \forall t \] (6)

after every iteration. Equation 2 was solved numerically using the toolset developed by Mitchell.\(^3\) With Eq. 2 solved, for each position \( x_b \in \partial G(t_b) \) we constructed a growth trajectory \( \gamma(x_b, t) \) via:

\[ \frac{d}{dt} \gamma(x_b, t) = -\partial_t \phi(x, t) \frac{\nabla \phi(x, t)}{||\nabla \phi(x, t)||} \] (7)

on the time interval \( t \in [t_b, t_f] \) subject to the initial condition that \( \gamma(x_b, t_b) = x_b \). As in our previous work, growth trajectories that merged/collided with other growth trajectories were excluded. The local growth distance, \( \Gamma(x_b) \), was computed as:

\[ \Gamma(x_b) = \int_{t_b}^{t_f} ||\dot{\gamma}(x_b, t)|| dt \] (8)

Finally, the local growth rate associated with position \( x_b \) was computed by dividing \( \Gamma(x_b) \) by the inter-visit time, \( t_f - t_b \).