

Surrogate endpoints in clinical trials of regenerative therapy

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Popular endpoints

- Contractile function
 - *Global*
 - *Regional*
- Vascular function
 - *Perfusion*
- Metabolic function
 - *Glucose uptake*
- Structural/morphological
 - *Viable tissue vs scar*
 - *Chamber volumes*



Considerations in assessing endpoints

- Predictive value for mortality and morbidity
- Insights into mechanism of action and/or pathophysiology
- Utility based on experience with drugs and devices

re·gen·er·a·tion *n.* “Regrowth of lost or destroyed parts or organs.”

The American Heritage® Dictionary of the English Language, 4th Edition ©2000

Criteria for regeneration

- growth of new healthy tissue
- improvement of function in regrown area



Popular endpoints

- | | <u>Predictive value/MOA insight</u> |
|--------------------------------|-------------------------------------|
| • Contractile function | |
| - <i>Global</i> | - <i>Fair/Poor</i> |
| - <i>Regional</i> | - <i>?/Good</i> |
| • Vascular function | |
| - <i>Perfusion</i> | - <i>?/Good</i> |
| • Metabolic function | |
| - <i>Glucose uptake</i> | - <i>?/Good</i> |
| • Structural/morphological | |
| - <i>Viable tissue vs scar</i> | - <i>Good/Excellent</i> |
| - <i>Chamber volumes</i> | - <i>Good/Good</i> |



Emerging insights

- Relevant morphological and functional endpoints required to establish therapeutic regeneration
- “Regeneration” used loosely to date; some cells may work clinically without inducing regeneration
- Predictive utility in regenerative applications not yet established; new guiding principles needed
- If regeneration improves clinical outcomes, then endpoints indexing regeneration may deserve particular attention going forward

