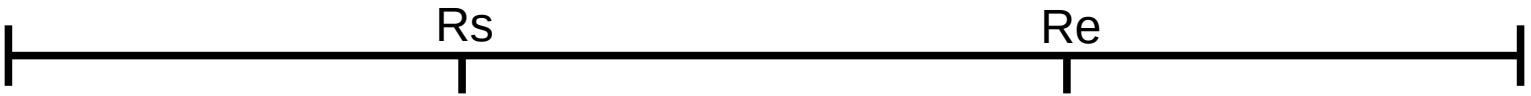
Overlap types

Defining feature-overlaps between sequences

Sequence-position definitions

- Reference Sequence
  - Rs is the **s**tarting location/position of a *feature* within the Reference
  - Re is the **e**nding location of a *feature* within the Reference
  - For the purposes of this exercise (case where Rs-Re is an intron) Re is always greater in number than Rs and location number on the sequence increases from left to right



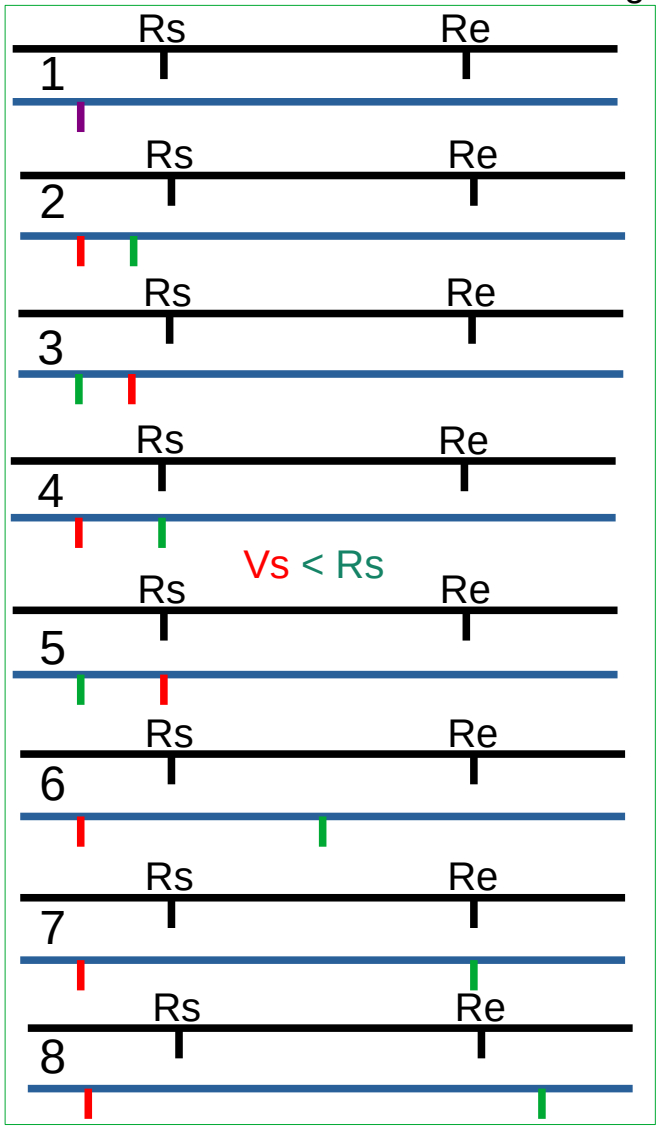
- Variant sequence
  - Vs is the starting location of a *feature* within the Variant
  - Ve is the ending location of a *feature* within the Variant
  - When Vs has a higher value than Ve it defines an *insertion* and Vs = Ve +1(always)

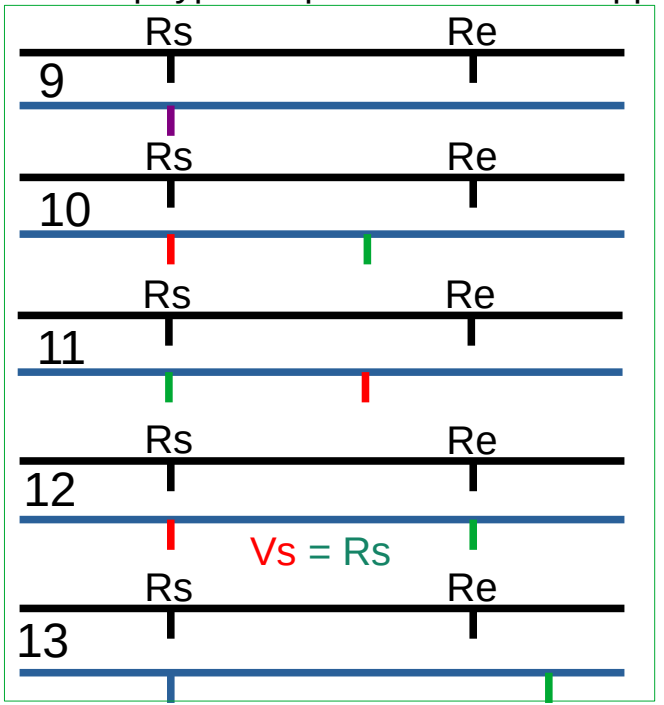
When Vs ==Ve, colour shown as purple

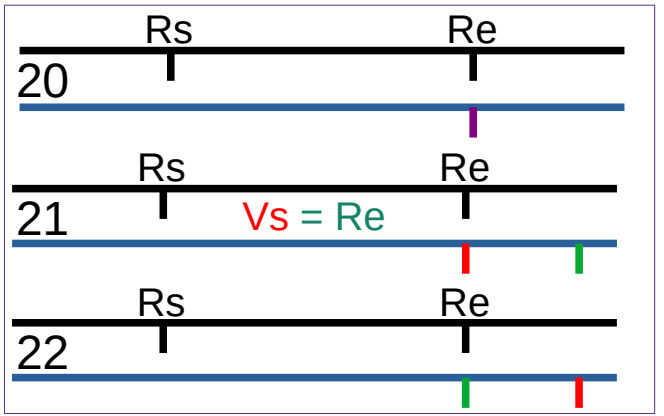
Overlap definitions

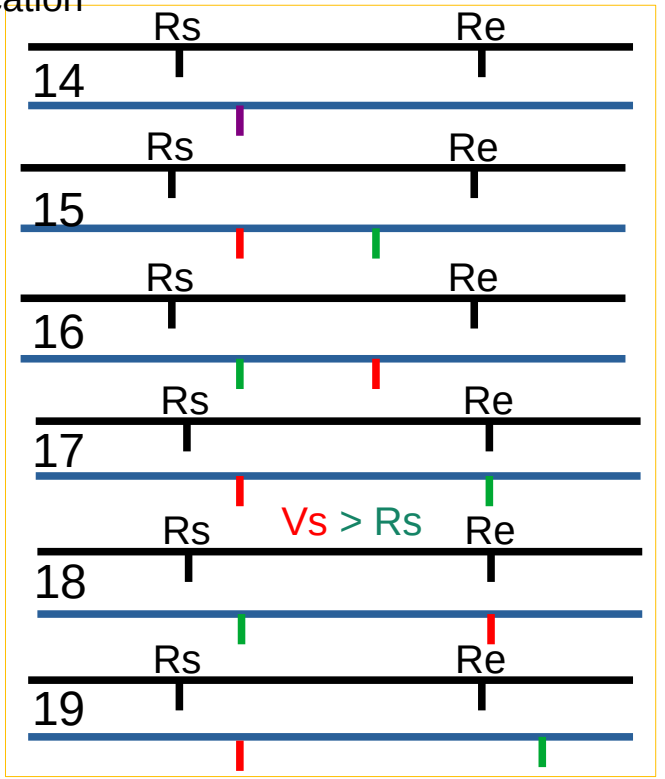
- The first iteration of this analysis (different number-set) was not systematic, missing cases where Vs = Ve.
- Second iteration considered only definitions where Re > Rs
  - Simply because the main case of interest is where the range Re ... Rs is an intron range.
  - This is called “skip” or “gap” in the code, to more generically describe the feature
  - The diagrams did not show a distinction in colour between Vs and Ve
- Third iteration shows a distinction in colour between Vs & Ve in diagrams
  - It thereby expands the number of cases to include where Vs = Ve + 1
  - Specifically the second-iteration cases 2, 3, 13, 16, 18 have another type
  - The other second-iteration cases do not have another type because these are clearly separated by > 1 given their relationships to Re & Rs
  - Eg: if one of the points Re or Rs lie between Vs & Ve, then it is impossible for Vs = Ve + 1
- Re … Rs effectively becomes a mask on the variants that are to be included
- Where a deletion crosses the skip-boundary, it must be detected to retain the part of the deletion that lies outside the range.

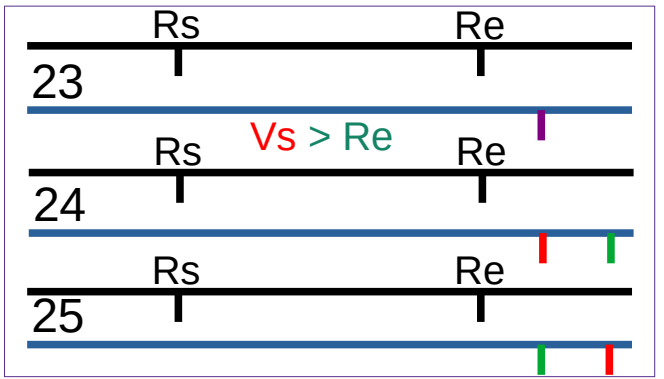
Numbering of overlap types implemented in the application





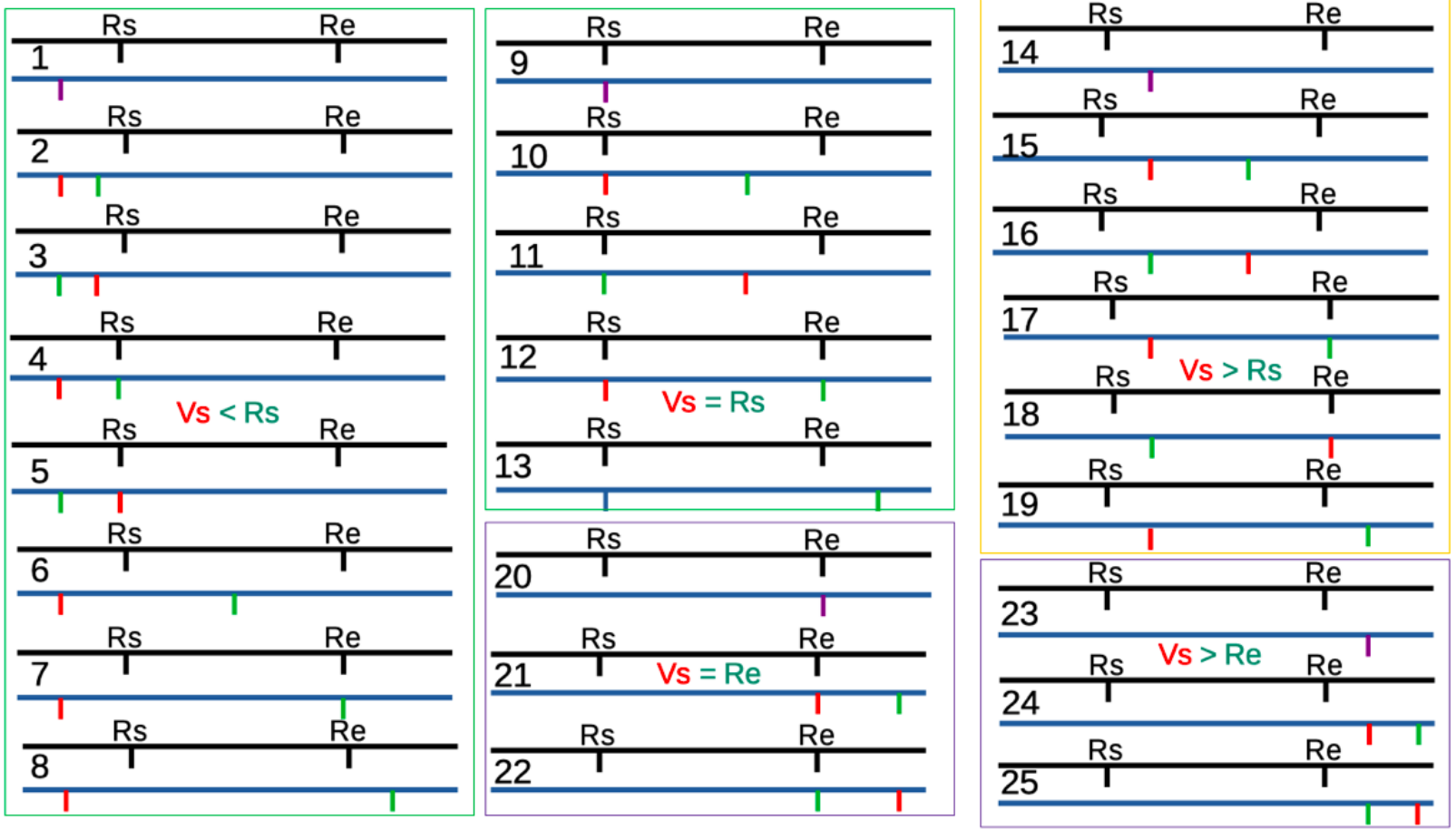






Overlap types between Reference and Variant features, as implemented

Rs is the **s**tarting location/position of a Reference feature; Re the **e**nd; eg: intron ranges
Vs is the starting location of a Variant *feature:*| ; Ve is the ending location |
When Vs==Ve ie: a SNP; point marked in purple: | ; Vs < Ve is a > 1 base substitution
When Vs > Ve it defines an *insertion* and Vs = Ve +1(always)



A number 1 to 25 is assigned to each different “Overlap Type”

Overlap types between Reference and Variant features, as implemented

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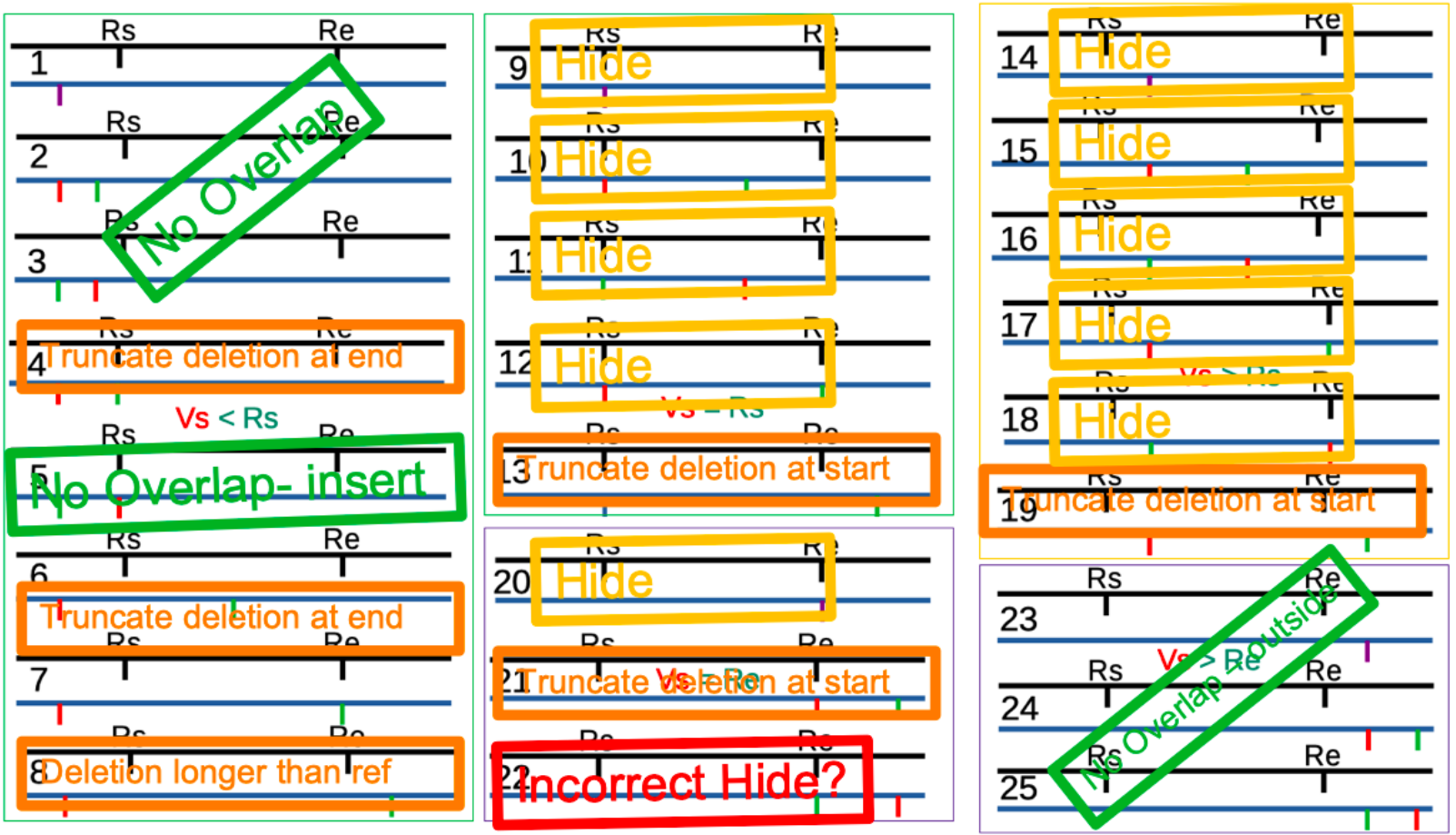
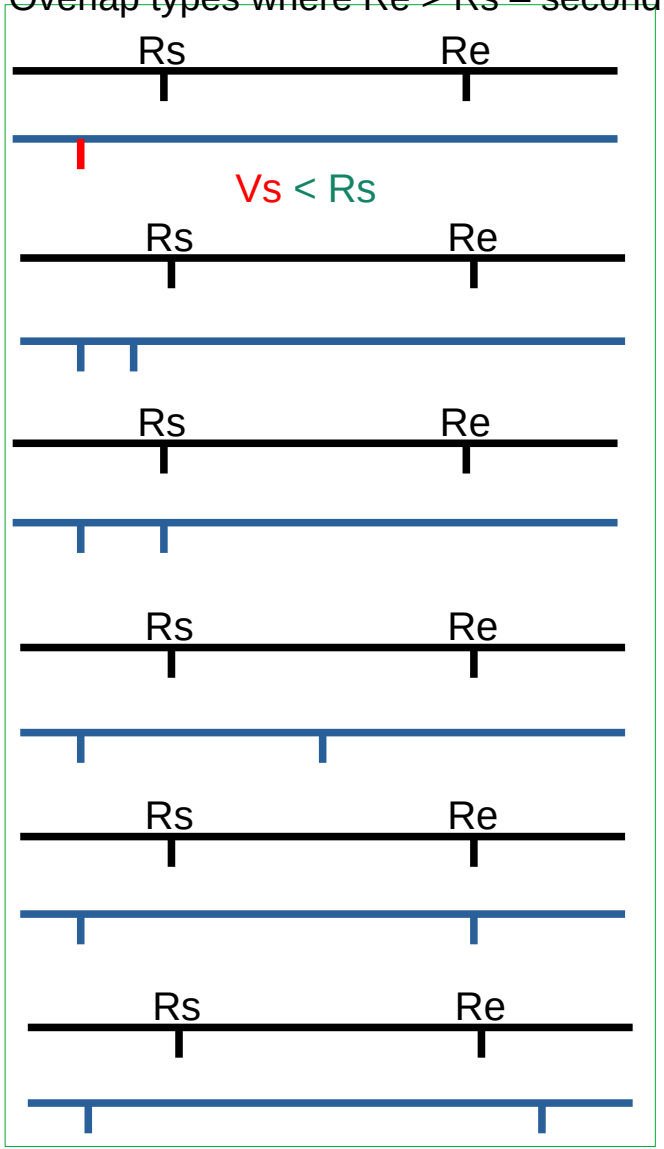


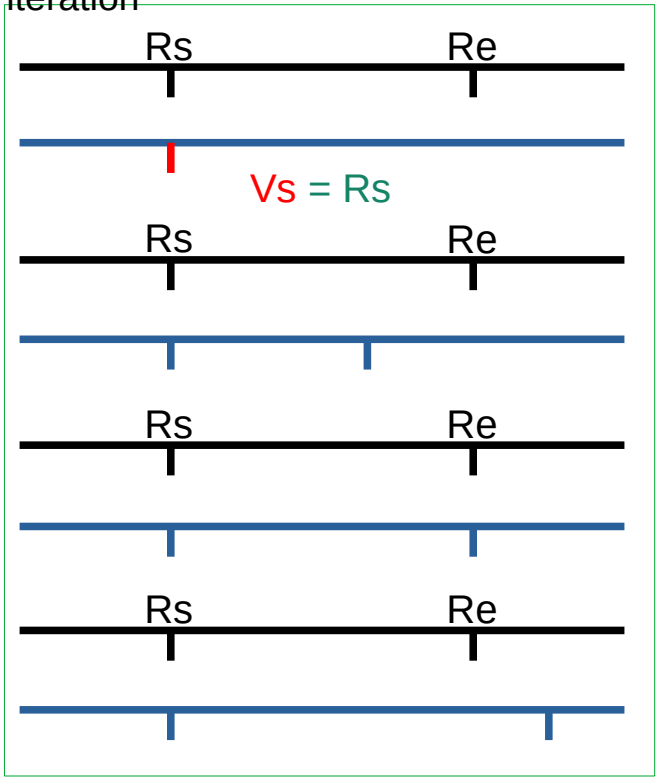
A number 1 to 25 is assigned to each different “Overlap Type”

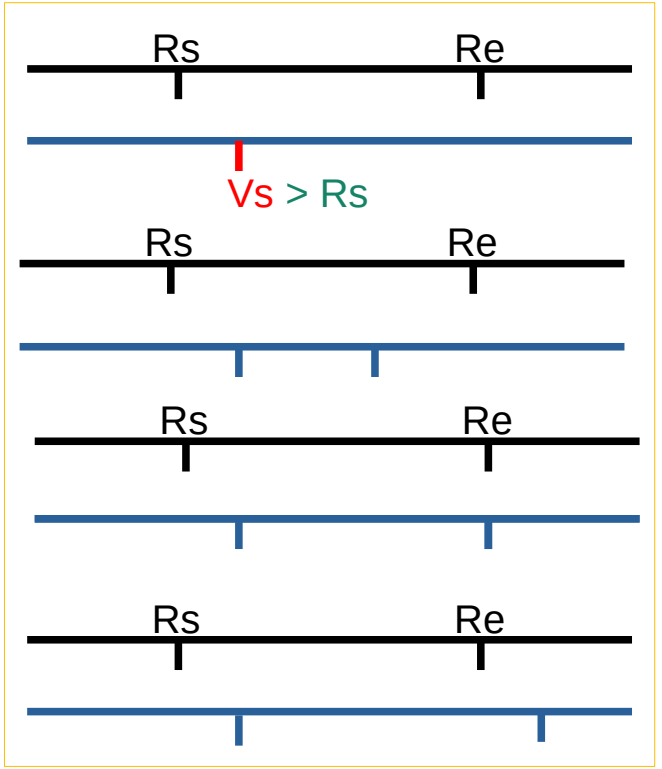
Older iterations documented

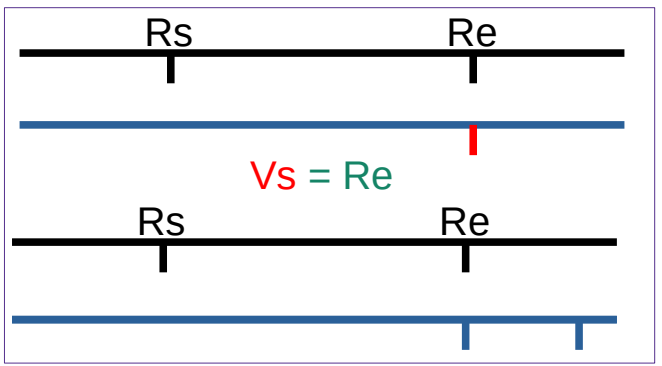
- Legacy documentation, tidied up

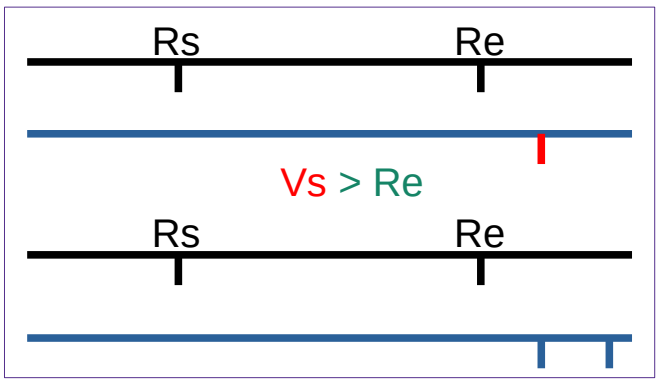
Overlap types where Re > Rs – second iteration



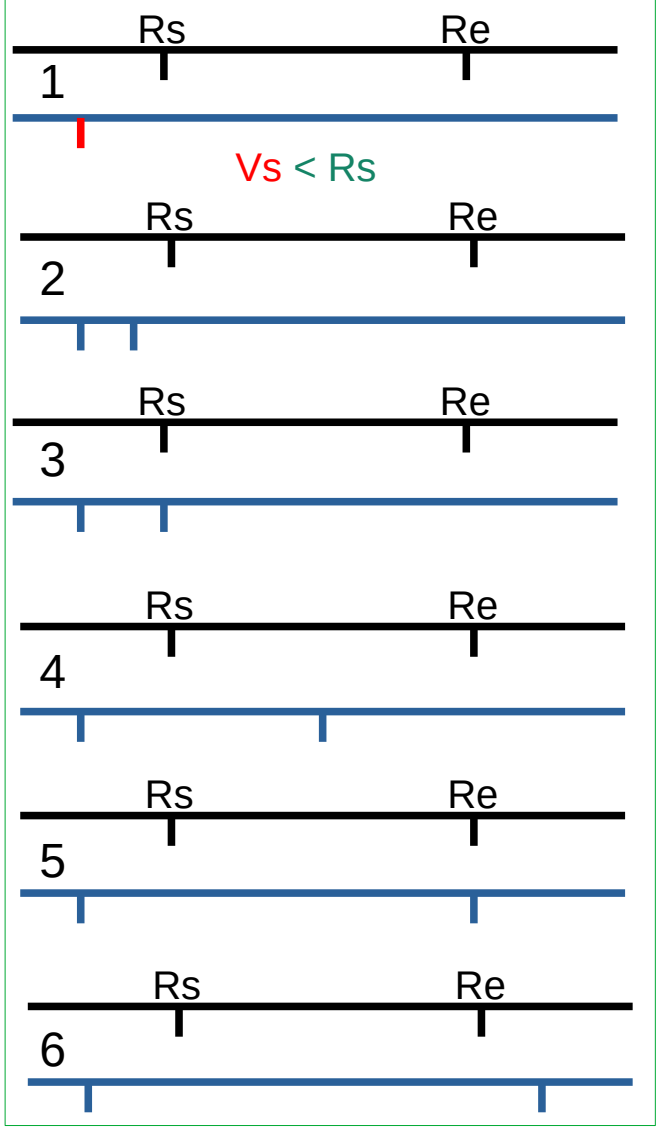


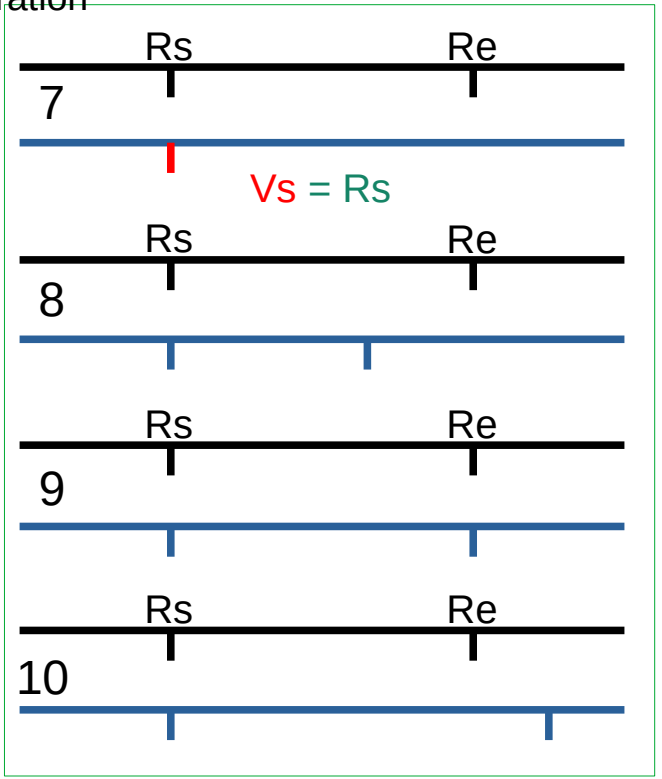


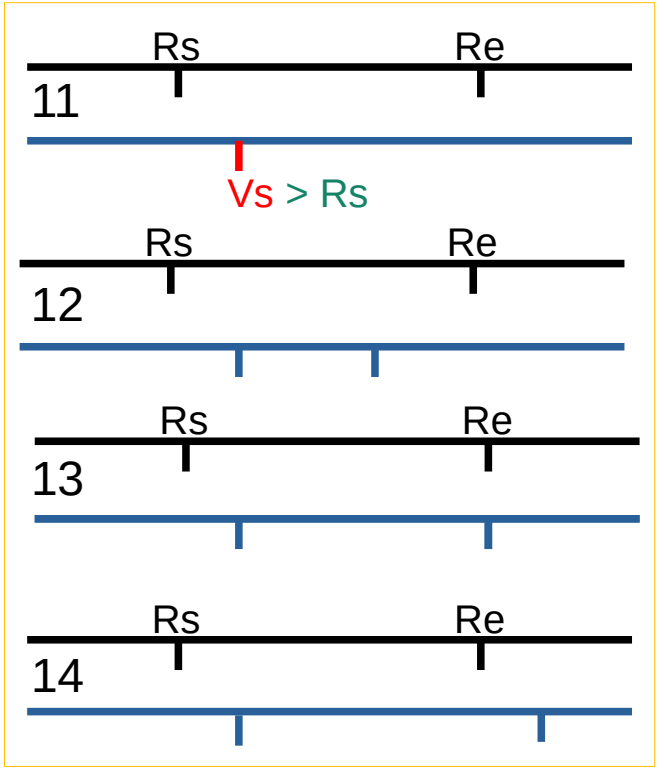


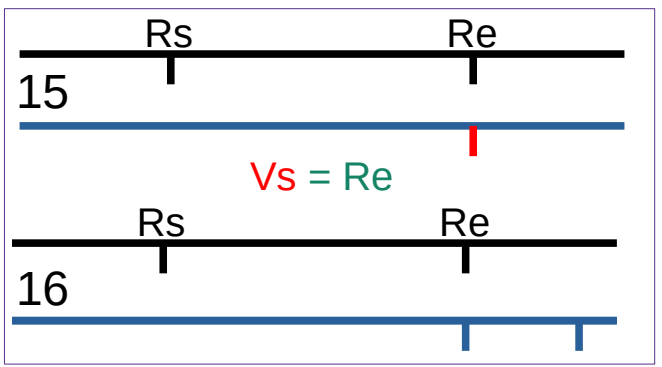


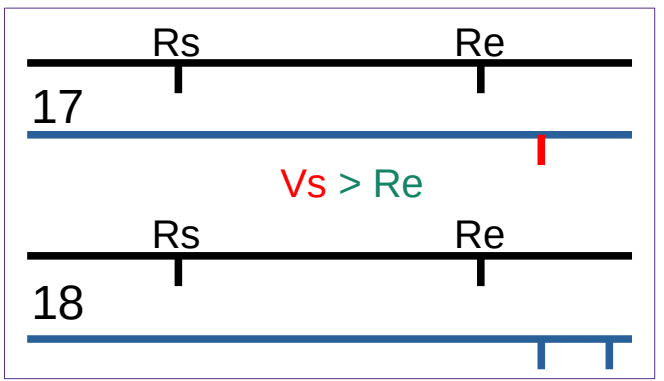
Numbering overlap types for second iteration





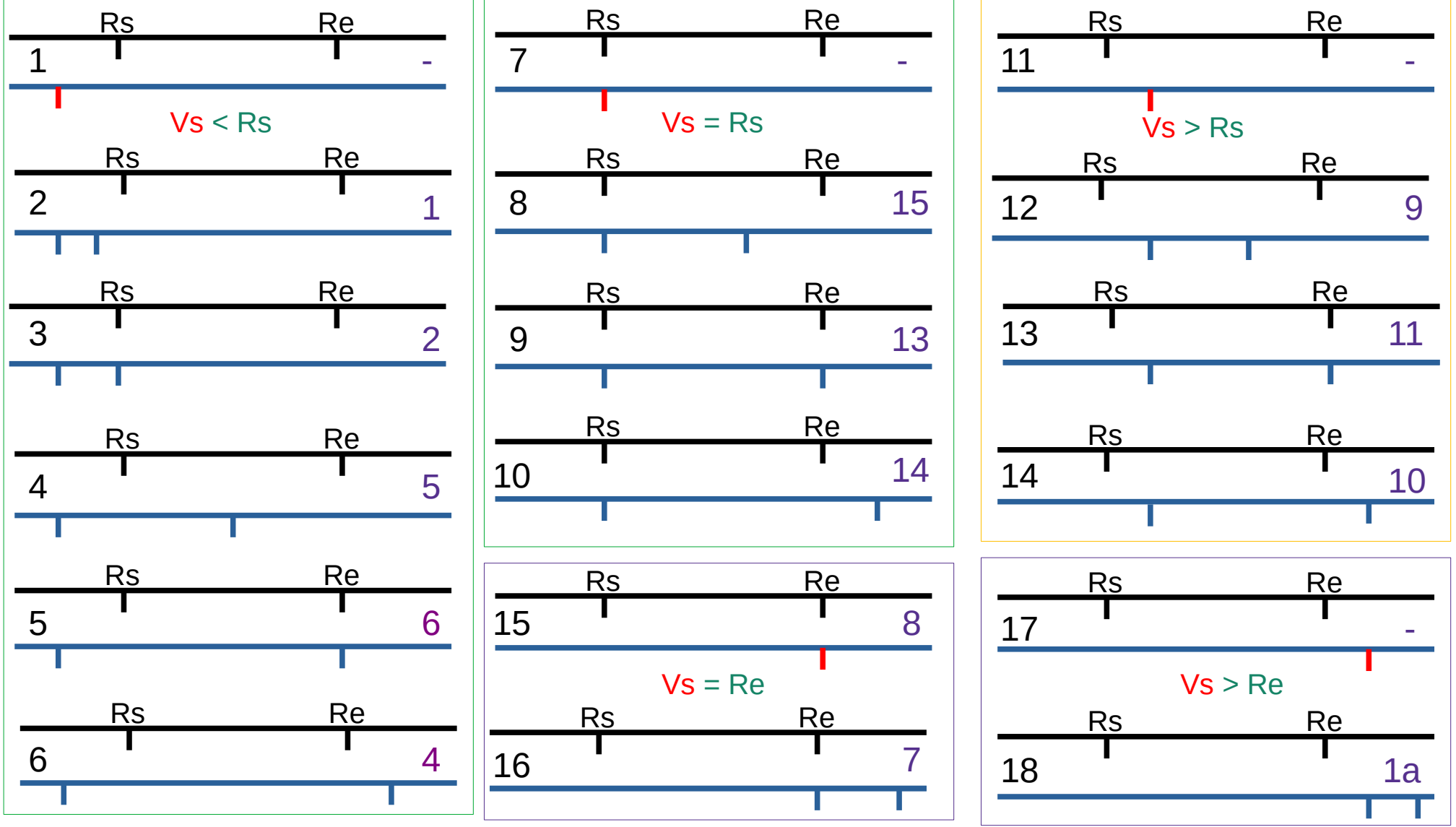


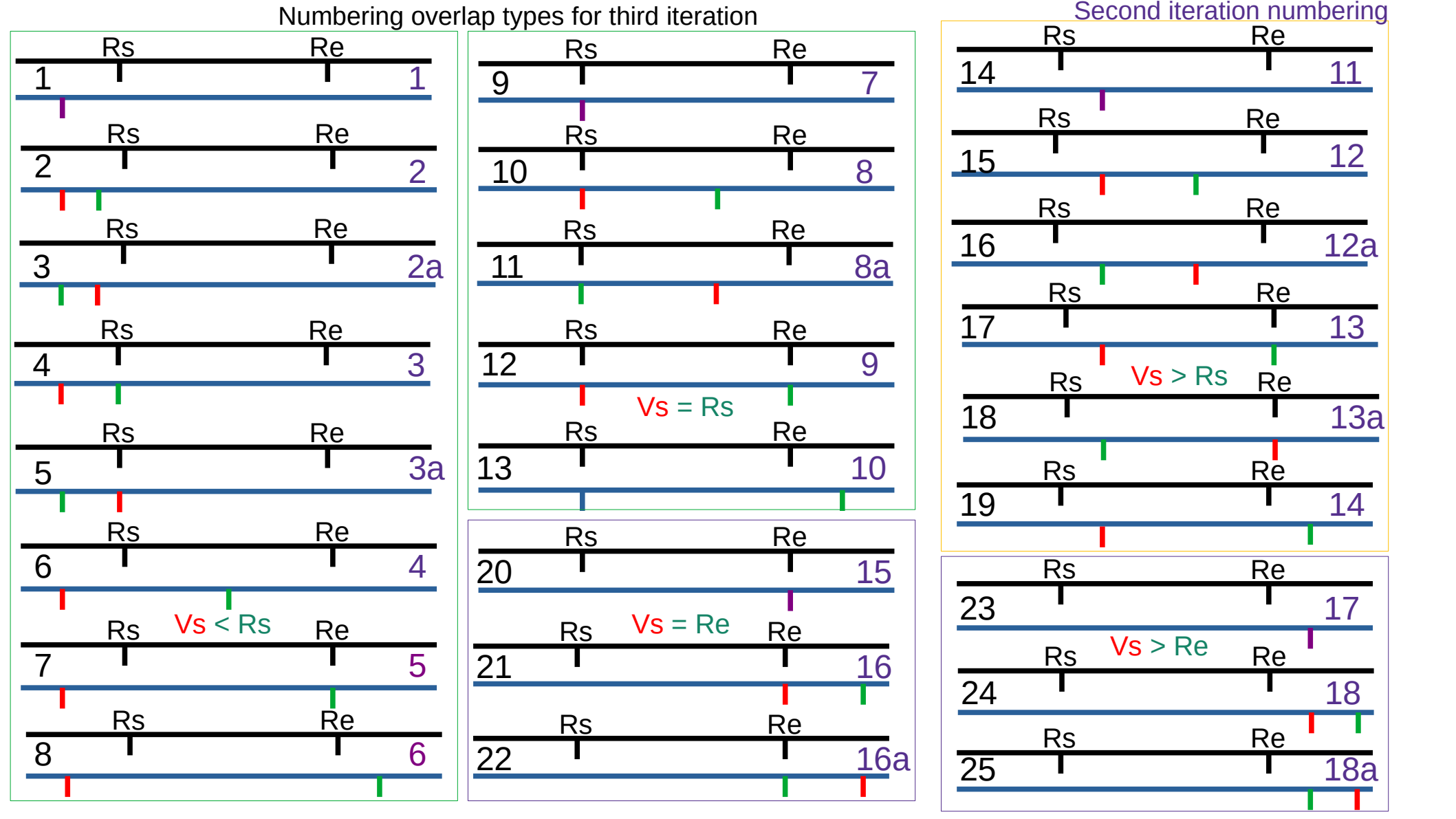




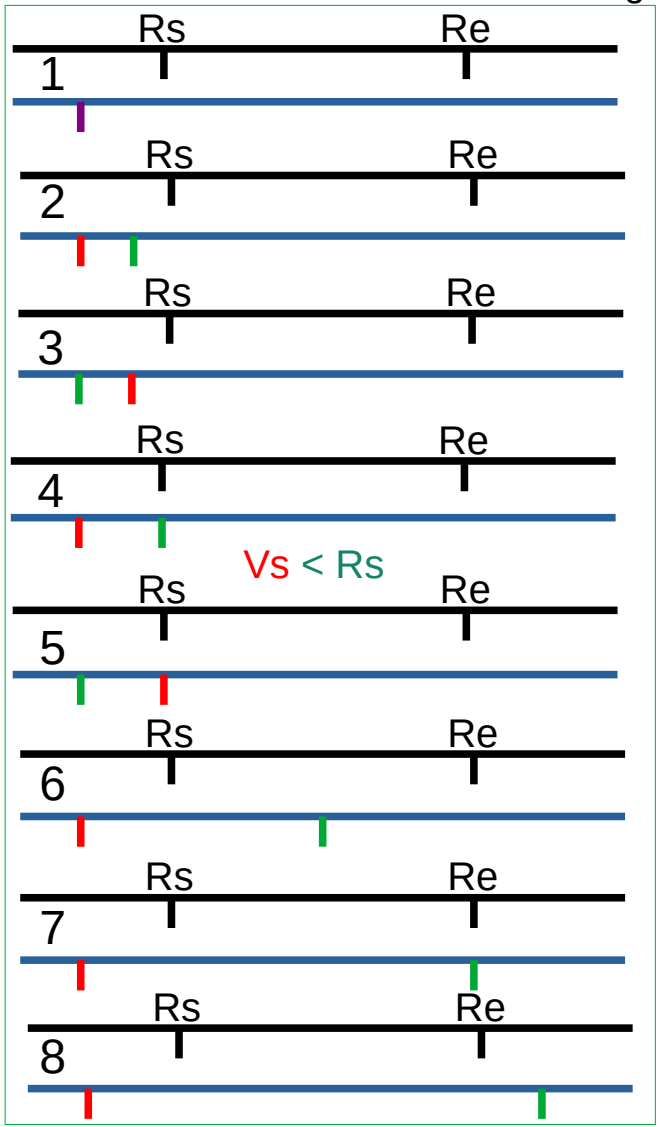
Numbering overlap types for second iteration

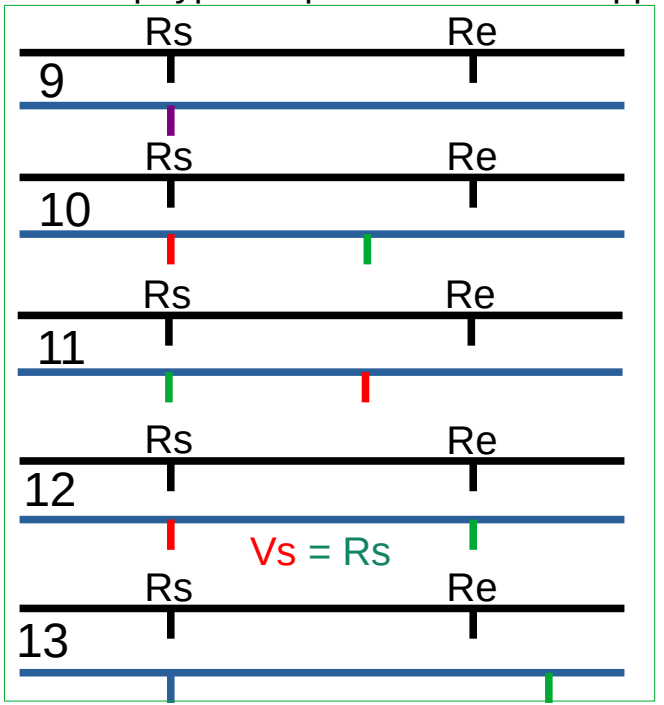
First iteration numbering

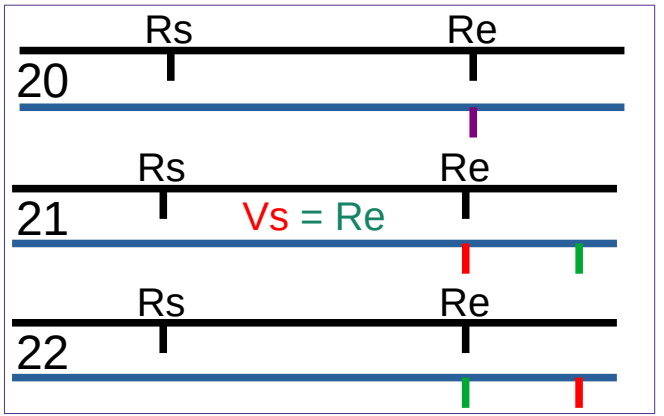


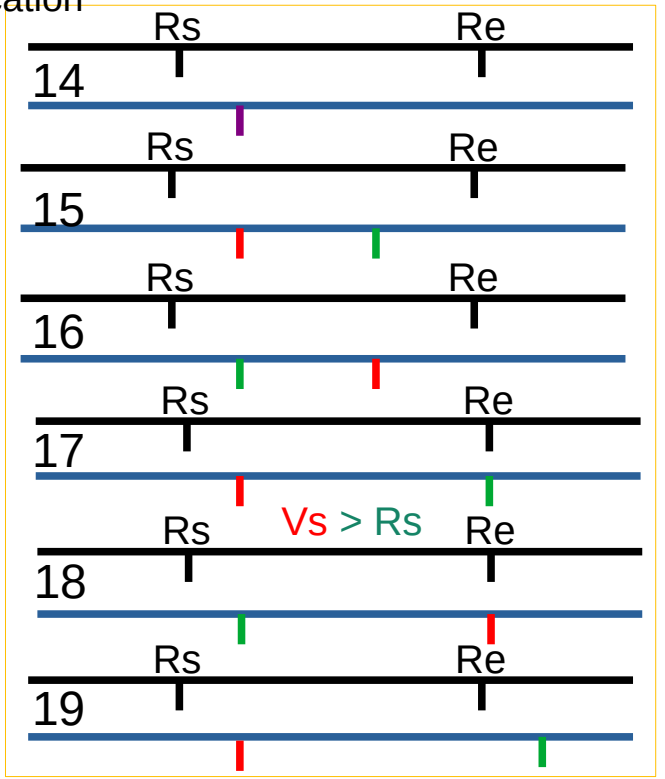

Numbering overlap types for third iteration
Second iteration numbering
Rs
Re
1
1
2
2
3
2a
4
3
5
3a
6
4
Vs < Rs
7
5
8
6
9
7
10
8
11
8a
12
9
Vs = Rs
13
10
20
15
Vs = Re
21
16
22
16a
14
11
15
12
16
12a
17
13
Vs > Rs
18
13a
19
14
23
17
Vs > Re
24
18
25
18a

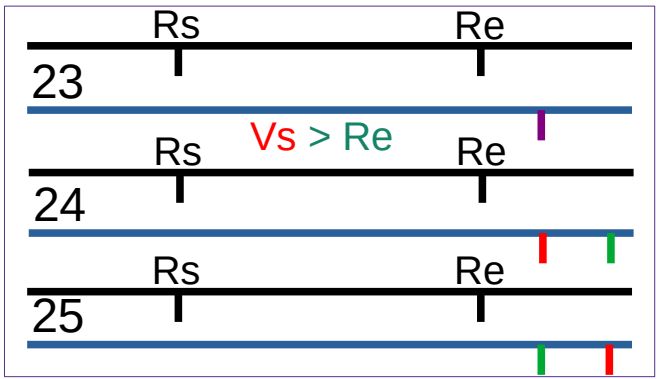
Numbering of overlap types implemented in the application











Annotated types

- The individual annotation of types is incomplete

Type 1

- Variant region is a point & precedes Reference
- No overlap

- FI: not defined ; SI: type 1 ; TI: type 1

Type 2

- Variant region precedes Reference
- No overlap

- FI: type 1; SI: type 2; TI: type 2

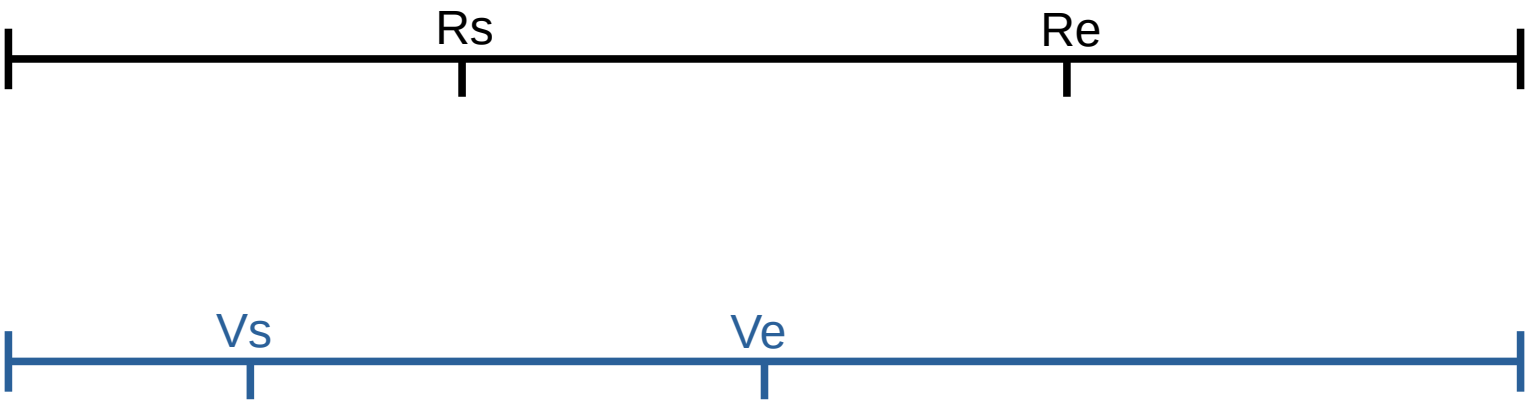
Type 4

- Variant concatenates start of Reference
  - (Vs < Rs) AND (Ve = Rs) AND (Re > Rs)

- FI: type 2; SI: type 3; TI: type 4

Type 6

- Variant begins before start of Reference, ends within Reference
  - (Vs < Rs) AND (Ve < Re)



  - Re > Rs not tested, but should be true when Ref feature is a skip (Re > Rs)
    - FI: type 5; SI: type 4; TI: type 6

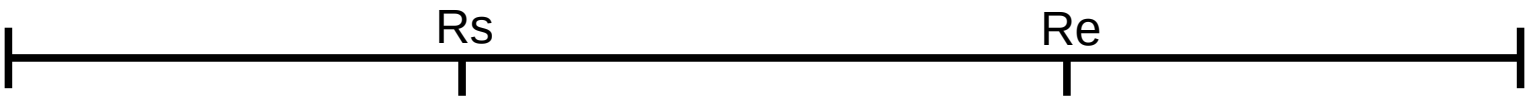
Type 7

- Variant begins before start of Reference
- Variant end coincides with Reference end
  - (Vs < Rs) AND (Ve = Re) AND (Re > Rs)

- FI: type 6; SI: type 5; TI: type 7

Type 8

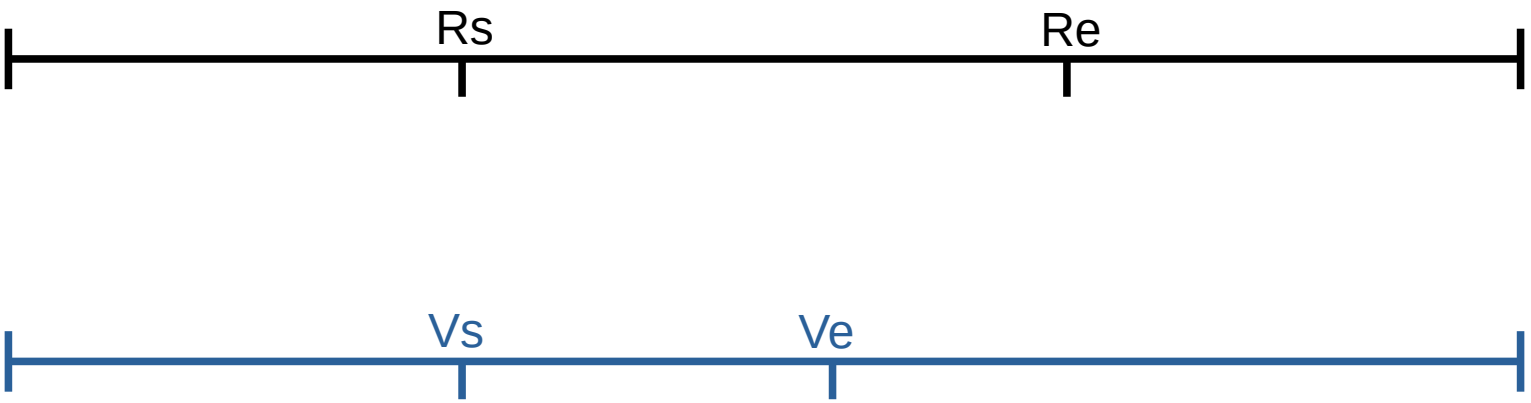
- Reference entirely contained within variant
  - (Vs < Rs) AND (Ve > Re)



  - Re > Rs not tested, but should be true when Ref feature is a skip (Re > Rs)
    - FI: type 4; SI: type 6; TI: type 8

Type 10

- Variant and Reference share start, ref longer than variant
  - (Rs = Vs) AND (Ve < Re)



- FI: type 15; SI: type 8; TI: type 10

Type 12

- Coincident feature positions
  - (Rs = Vs) AND (Re=Ve)

- FI: type 13; SI: type 9; TI: type 12

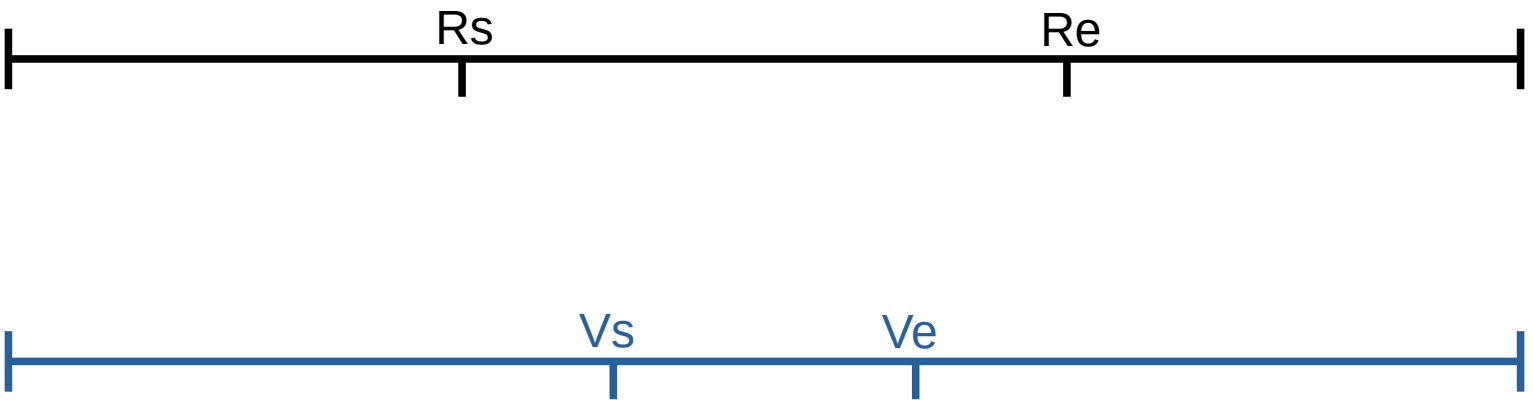
Type 13

- Variant and Reference share start, variant longer than ref
  - (Rs = Vs) AND (Ve > Re)

- FI: type 14; SI: type 10; TI: type 13

Type 15

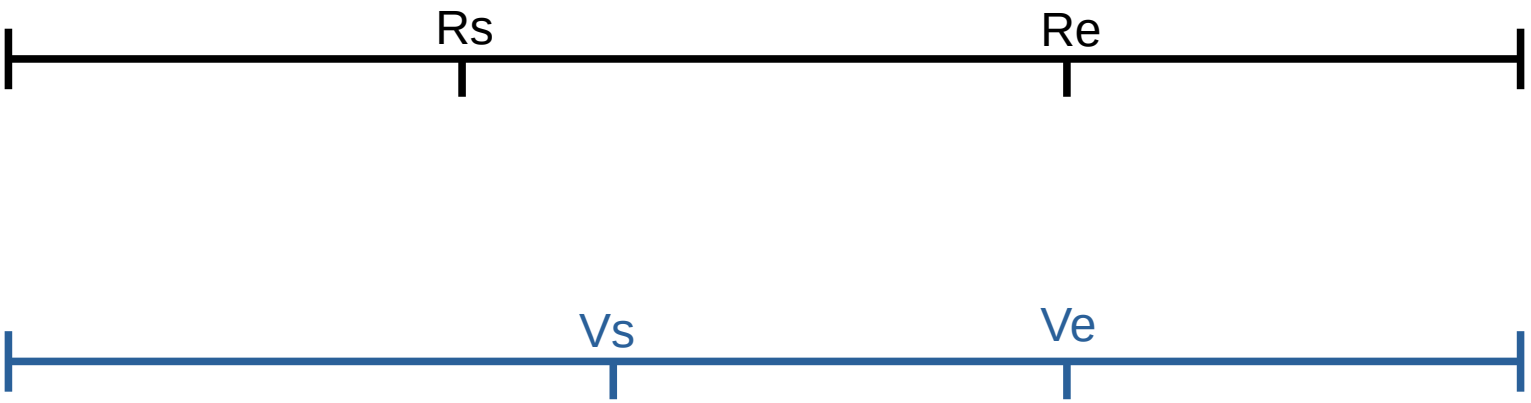
- The Variant range is entirely within the Reference range
  - (Re > Vs) AND (Ve < Re)



  - Re > Rs not tested, but should be true when Ref feature is a skip (Re > Rs)
    - FI: type 9; SI: type 12; TI: type 15

Type 17

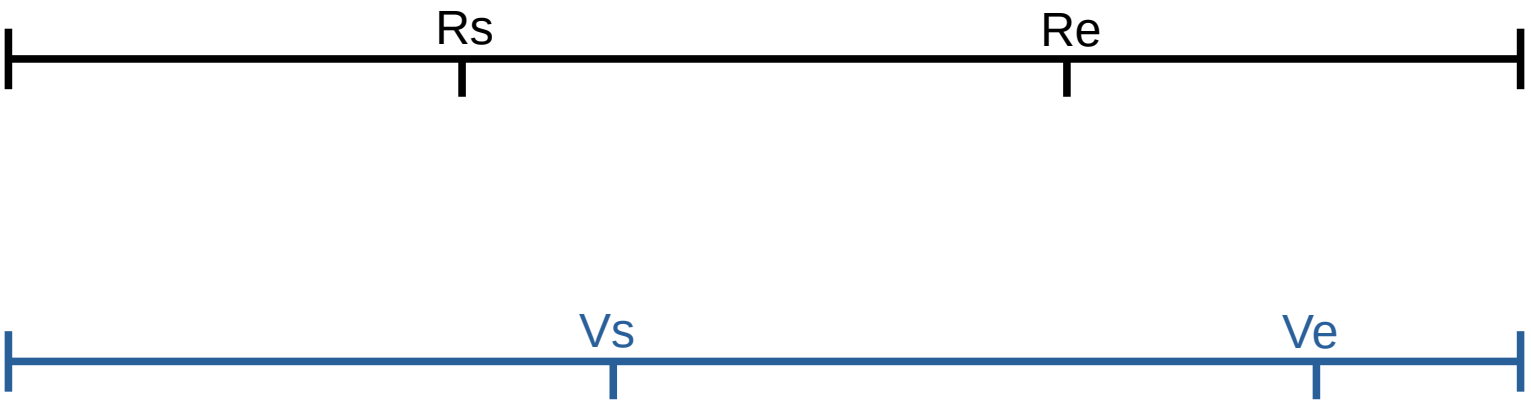
- Variant range entirely within reference, but ends coincide
  - (Re > Vs) AND (Ve = Re)



- FI: type 11; SI: type 13; TI: type 17

Type 19

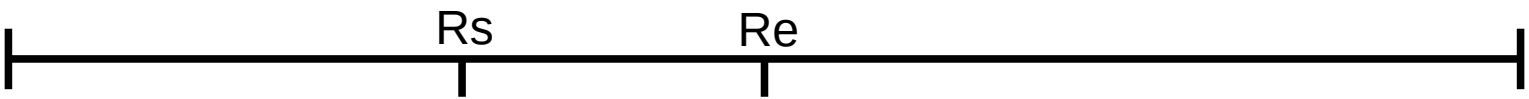
- Variant begins within Reference range but ends after Reference end
  - (Re > Vs) AND (Ve > Re)



  - Re > Rs not tested, but should be true when Ref feature is a skip (Re > Rs)
    - FI: type 10; SI: type 14; TI: type 19

Type 20

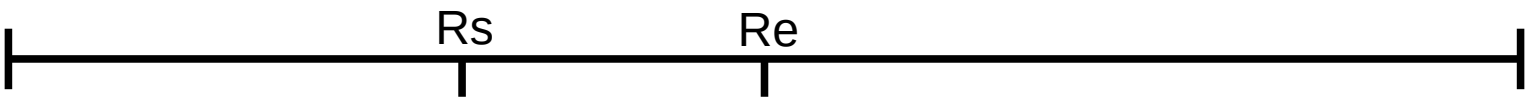
- Variant is a point coinciding with Reference end
  - (Vs > Rs) AND (Re = Vs) AND (Ve = Vs)



  - Re > Rs not tested, but should be true when Ref feature is a skip (Re > Rs)
    - FI: type 8; SI: type 15; TI: type 20

Type 21

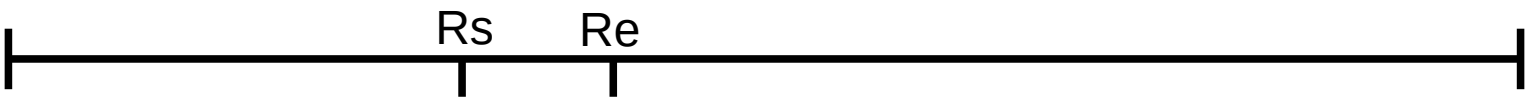
- Variant start coincides with Reference end
  - (Vs > Rs) AND (Re = Vs) AND (Ve > Vs)



  - Re > Rs not tested, but should be true when Ref feature is a skip (Re > Rs)
    - FI: type 7; SI: type 16; TI: type 21

Type 24

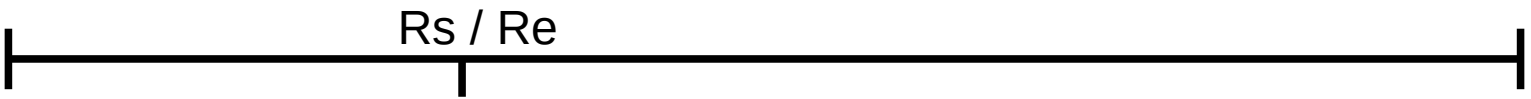
- Variant region after Reference
- No overlap
  - (Vs > Rs) AND (Re < Vs)



  - Re > Rs not tested, but should be true when Ref feature is a skip (Re > Rs)
    - FI: type 1A; SI: type 18; TI: type 24

Not defined (1)

- Variant concatenates start of Reference
- Reference is a point
  - (Vs < Rs) AND (Ve = Rs) AND (Re = Rs)



  - Does not occur when Ref feature is a skip (Re > Rs)

    - FI: type 3; SI and TI: not defined

Not defined (2)

- Coinciding points on both Variant and Reference
  - (Rs = Vs) AND (Vs = Re) AND (Vs=Ve)
  - 

  - Should not occur when Ref feature is a skip (Re > Rs)
    - FI: type 12; SI and TI: undefined