Methods of minimal residual disease assessment in acute myeloid leukemia

	Sensitivity	Advantages	Disadvantages
Conventional karyotyping	5%	• Common in routine clinical practice	• Poor sensitivity • Time consuming and labor intensive • Applicable only to patients with baseline abnormal karyotype (~50%)
Fluorescent *in situ* hybridization	Up to 10^{-2}	• Useful for numeric cytogenetic tabnormalities (i.e. gains or • deletions)	• Worse sensitivity than MFC or PCR • Applicable only to patients with baseline abnormal karyotype (~50%)
Multiparameter flow cytometry for LAIPs* or DfN**	10^{-3} to 10^{-5}	• Sensitive • Fast (results usually available within 24 h) • Relatively inexpensive • Applicable to >90% of AML cases	• Potential for immunophenotypic shifts (mitigated by using DfN-based approach) • Requires significant technical expertise to interpret • Limited standardization across laboratories
RT-qPCR	10^{-4} to 10^{-6}	• Sensitive • Well standardized • Can be run in any laboratory with RT-qPCR capabilities • Applicable to >90% of AML cases	• Appropriate molecular targets present in <50% of cases (<35% in older adults) • Many mutations are not suitable for MRD detection (e.g. FL T3) • Time consuming and labor intensive • Results may take several days
Next-generation sequencing	Highly variable (1% to 10^{-6})	• Potential for very high sensitivity (depending on technology) • Can test multiple genes at once	• Low sensitivity with most commonly used platforms • May be confounded by persistence of preleukemic mutations (e.g. CHIP) • Results may take several days • Expensive • Not standardized • Requires complex bioinformatics

*LAIPs: leukemia-associated immunophenotypes
**DfN: difference from normal analysis

Short and Ravandi, Haematologica, 2019